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MANAGEMENT OF COUGH IN DAILY PRACTICE

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Cough is one of the most frequent symptoms for which the patient seeks medical attention. Although cough can be produced voluntarily, it is, in its spontaneous form, a reflex function of the body. Its purpose is the removal of accumulated mucus, inflammatory exudates, products of circulatory stagnation, extravasated blood, or foreign bodies from the respiratory tract and to rid the body of irritation of any sort originating in the air passages. Its most frequent sources are diseases of the lung, the throat, and the heart. For the intelligent and efficient treatment of cough, it is mandatory to search for its cause and institute appropriate measures accordingly. The multiplicity of lesions that may elicit cough should be recognized. Pathological changes in any part of the respiratory system, whether of mechanical, toxic, infectious, allergic, neoplastic, or other origin, may provoke cough.

It is reasonable to assume that the forces of coughing are capable of evacuating inflammatory products or foreign bodies from the respiratory tract. In case of an inflammatory disease of the lung, such as bronchitis or pneumonia, one would expect a successful drainage under the effect of cough. If this is actually accomplished by coughing, one considers the cough as useful, adequate, or beneficial. There are a number of instances, however, when cough is not productive of any sputum or when the amount of sputum expectorated is much less than the coughing effort should have produced. This type of cough is customarily designated as unproductive or useless (tussal insufficiency).

TUSSAL INSUFFICIENCY

Useless or inadequate cough may be brought about by the following circumstances:

1. The source of irritation that initiates the cough reflex is outside of the lung, as for instance in diseases of the paranasal sinuses, an elongated uvula, pressure on the trachea or bronchi by mediastinal inflammation, tumors, or dilated blood vessels.

2. Noninflammatory lesions of the bronchial tubes, such as benign or malignant tumors, may cause persistent, annoying cough without expectoration.

3. During the course of a great many inflammatory involvements of the bronchi or the lung parenchyma there is a phase when the formation of exudate is practically nil; nevertheless, the congested state of the involved structures leads to strenuous but useless cough. The best examples of this are the first stage of an acute bronchitis with a so-called dry cough and certain forms of allergic bronchitis.

4. A frequent source of inadequate cough is any disease of the lung in which the mucoid or mucopurulent products of inflammation are so tenacious, sticky, and adherent to the walls of the respiratory passages that even intense, exhaustive coughing is unable to remove them. The prototype of inadequate cough of this sort is that seen in the paroxysmal stage of whooping cough.

5. Accumulation of too much transudation in the alveoli in heart failure may elicit coughing that is insufficient for the cleansing of the lung.

6. There are cases in which retention of pulmonary exudates is taking place because their removal is blocked by pathological structural changes such as the formation of bronchial strictures. Such a condition often causes strenuous but ineffective coughing.

7. Atelectasis may be the source of useless cough for the reason that, when the lung becomes airless distal to inflamed areas, there is no chance for the inspired air to get behind the inflammatory products that accumulate in the corresponding bronchial tubes; therefore, it cannot be compressed and act as the normal expulsive force of coughing.

8. Useless cough is common in pulmonary emphysema.

Assuming that there is inflammatory exudation in the lungs, its removal either by resorption or by expectoration is essential for the restoration of the normal anatomical and functional status of this organ. In the presence of tussal insufficiency, an accumulation and retention of mucus and purulent exudate may take place. The stagnation of inflammatory products in the bronchi and bronchioles is dangerous. The retained material may coagulate in the air passages, including the alveoli. Thus

it may cause complete obstruction and consequent atelectasis in the corresponding distal segment of the lung. Atelectasis obviates free motion of the respective lung areas. In the absence of normal lung motion, the flow of lymph is reduced or absent too. For this reason, exudate will not be carried through the implicated lymph channels but will coagulate therein. Coagulated exudate has a tendency to heal by fibrosis, with ultimate damage to the integrity of the lung tissue. Pathogenic micro-organisms that are dominant in the retained mucopus are likely to lead to pathological changes in the surrounding bronchial walls and consequently may cause bronchiectasis.

Tussal insufficiency may entail other difficulties. Drop-lets of purulent, thin exudate may be sprayed from one segment of the lung to another or from one lung to the opposite side.

Tussal insufficiency associated with severe coughing increases the metabolic rate and interferes with the rest of the patient and with the rest of the lungs. Pulmonary hemorrhage may be initiated by excessive, strenuous cough. Other possible disagreeable sequelae of severe coughing include spontaneous pneumothorax, vomiting, loss of appetite, exhaustion, headache, insomnia, rise in temperature, marked dyspnea, cyanosis, thoracic pain, fracture of ribs, mediastinal emphysema, subcutaneous emphysema, subconjunctival hemorrhage, urinary incontinence, and, indirectly, myocardial failure. Strenuous, protracted, unproductive cough affects the heart adversely, because the high intrapulmonary pressure represents an impediment to pulmonary circulation. This is particularly true of the aged. Roentgenograms of the chest taken during the Valsalva experiment (forced attempt at expiration with the glottis closed) show that the blood content of the lung is greatly reduced, owing to the fact that the right ventricle is unable to overcome the high intrapulmonary pressure.

In chronic infections of the lung, the elastic fibers of this organ may become weakened either by toxic influences or by interference with their normal blood supply. The latter is brought about by perivascular fibrosis secondary to chronic infection. McCann and his associates¹ demonstrated that during severe coughing spells the intrapulmonary pressure rose to 200 mm. of mercury (270 cm. of water) over atmospheric pressure. Excessive increase in the intrapulmonary pressure during the course of protracted pulmonary infections is bound to break the

weakened elastic fibers of the lung. Extensive loss of pulmonary elastic fibers results in hypertrophic emphysema.

TREATMENT

Tussal insufficiency is treated symptomatically by cough sedatives when there is no material in the lower air passages that requires removal. Codeine (methylnorphine) and dihydrocodeinone bitartrate are preferable for this purpose. Both are capable of sedating the respiratory center without causing depression of higher centers in the brain when administered in standard medicinal doses. Dihydrocodeinone bitartrate, a derivative of codeine, is a white, crystalline powder, freely soluble in water. Since 1923, a number of reports have dealt with its pharmacologic properties and clinical application.² I have found that it had a prompt antitussive action without interfering with the expectoration of inflammatory products. It is a habit-forming drug. In this respect, its potentialities are less serious than those of morphine but they are worse than those of codeine. Nausea may be a complaint when the drug is taken on an empty stomach. Dihydrocodeinone bitartrate is administered in the following dosage: adults, 5 to 10 mg. ($\frac{1}{12}$ to $\frac{1}{6}$ grain) three times within a 24-hour period; children 2 years of age or older, one-half the adult dose; younger children, one-quarter the adult dose. When circumstances require, the drug may be given subcutaneously.

The use of morphine is hardly ever justifiable in the management of cough. In addition to its highly habit-forming tendency, a number of its properties make its administration objectionable in the treatment of cough:

1. It depresses the respiratory center too much. Consequently, the respiratory excursions of the chest and the respiratory volume of the lung diminish. These changes, in turn, imply a decrease in the normal expansion and contraction of the bronchi. In addition, the bronchial peristalsis is slowed down. The untoward effect of such chain of events on the normal cleansing capacity of the lower respiratory tract is self-evident.

2. Morphine diminishes the muscular tone of striated muscles, including the diaphragm. The latter is responsible for 37% to 47% of the ventilatory function of the lung and in a large measure for the normal cough mechanism. Weakening of the functional capacity of the diaphragm inevitably interferes with the efficacy of cough.

3. Morphine exerts an inhibitory action on the glands of the bronchial mucous membrane. Such interference with the physiological function of the bronchial mucosa represents another handicap in the way of the normal evacuation of bronchi. Also, it is well to keep in mind that undue dryness of the mucosal surface renders it more irritable, and it is therefore liable to increase the cough.

4. Morphine causes a spasm of the smooth muscles of the bronchi and bronchioles. This, in turn, implies disturbed bronchial peristalsis (bronchial dyskinesia). The electrobronchographic studies of Luisada³ illustrate that the oscillations of the normal pattern disappear after the administration of morphine.

1. McCann, W. S., and others: Tussive Syncope; Observations on Disease Formerly Called Laryngeal Epilepsy, with Report of 2 Cases, *Arch. Int. Med.* 84: 845, 1949.

2. Hecht, P.: Clinical Investigation of Cough Remedies of the Morphine Group, *Klin. Wchnschr.* 2: 1069, 1923. Schindler, R.: Clinical Experience with Dicodeid, a New Compound of the Morphine Group, *Muenchen. med. Wchnschr.* 70: 467, 1923. Kaupé, W.: Dicodeid in Children, *Med. Klinik* 20: 1467, 1924. Myers, G. N.: Investigation on the Pharmacological Action of Some New Substitutes for Morphine and Heroin, *Brit. M. J.* 2: 282, 1933. Wright, C. I.: Respiratory Effects of Morphine, Codeine and Related Substances; Effect of Dihydrocodeine, Dihydroisocodeine, Dihydroallopseudocodeine and Dihydrodipseudocodeine, *J. Pharmacol. & Exper. Therap.* 51: 343, 1934. Stein, P., and Lowy, P.: Hycodan; Dihydrocodeinone, *Am. Rev. Tuberc.* 53: 345, 1946. New and Nonofficial Remedies: Dihydrocodeinone Bitartrate, report of the Council on Pharmacy and Chemistry, *J. A. M. A.* 138: 820 (Nov. 13) 1948.

3. Luisada, A.: Experimental Studies on the Function of the Smooth Muscles of the Lung, *Boll. d. Soc. ital. di biol. sper.* 3: 434, 1928; *Beitr. z. Klin. d. Tuberk.* 73: 657, 1930 and 77: 460, 1931; *Pulmonary Dynamics, Ergebn. d. inn. Med. u. Kinderh.* 47: 92, 1934; *Ztschr. f. d. ges. exper. Med.* 90: 800, 1936.

The only exceptions to the contraindication to the use of morphine in the management of cough are (1) inoperable tumors of the lung and mediastinum when the cough cannot be controlled by other means or when it is associated with otherwise uncontrollable pain, (2) aneurysm of the aorta, pressing on the trachea or bronchi, provided the cough cannot be checked by other cough sedatives, and (3) certain cases of cardiac decompensation with cough in which sometimes surprisingly gratifying relief from respiratory distress and cough can be achieved by morphine.

Of the saline expectorants, ammonium chloride is the most widely used. It is easily soluble in water. It should not be prescribed in alkaline solutions because it becomes decomposed. The experimental observations of Perry and Boyd⁴ demonstrated that ammonium chloride increased the respiratory tract fluid through its reflex action from the stomach. When the branches of the vagus supplying the stomach were cut, ammonium chloride introduced into the stomach was ineffective. Under ordinary circumstances the increased bronchial secretions dilute and soften the inflammatory exudate and thereby aid its easier evacuation. Because of its diluting action, this and related salts are described as "solvent expectorants." They are used to advantage in the so-called tight cough, which is not competent to remove the scanty, tenacious mucus from the bronchi. Their chief indication is the presence of troublesome cough during the acute and subacute phases of infections of the lower respiratory tract, such as bronchitis, bronchopneumonia, and lobar pneumonia. Also, in long-standing pulmonary tuberculosis these drugs may effectively increase the fluid secreted in the bronchi so that viscid, adherent mucus is liquefied and moved out. Basch and his associates⁵ investigated the characteristics of bronchial secretions after the administration of ammonium chloride. They noted a lowering of the viscosity and the pH and an increase in the dried residue and the total nitrogen content. In addition to increasing the fluidity of the bronchial secretions, ammonium chloride stimulates the ciliary function of the mucous membrane. No satisfactory results can be expected unless ammonium chloride is given in large enough doses. For this reason it is best to prescribe 5 grains (0.3 gm.) every two hours, or even every hour if necessary.

Potassium iodide is one of the most effective compounds for the dilution and liquefaction of viscid mucopurulent products in the bronchial tubes. Experimental observations of Tuft and Levin⁶ show that it is excreted through the bronchial mucosa in 15 to 25 minutes whether it is given orally or intravenously. In this respect, intravenous administration has no advantage over the oral one. Its excretion is accompanied by a hyperemia of the mucous membrane and by an increase in the secretion of the bronchial glands. Consequently, the adherent inflammatory exudate becomes more watery and less tenacious. Basch, Holinger, and Poncher⁷ reported their chemical studies on this subject. They noted that, after the administration of potassium iodide, the viscosity and pH of the sputum were lowered. Changes in the dried residue, the amount of ash, and the total nitrogen

content were variable. Potassium iodide is administered in the form of enteric coated tablets of 7½ or 15 grains (0.5 to 1.0 gm.), as a solution in one of the syrups used as flavoring vehicles, or as a saturated watery solution of the salt.

The experimental studies of Perry and Boyd⁴ show that, through its reflex action initiated in the stomach, ipecac is capable of increasing the secretions of the glands of the bronchial mucous membrane. The increased secretions dilute the viscid inflammatory products and thus assist in their dislodgement and removal from the respiratory passages. The emetine and saponin content of ipecac are considered responsible for its therapeutic influence. Basch and his collaborators⁵ studied the effect of fluid extract of ipecac. They recorded that the viscosity of the sputum was lowered but its pH was not influenced. Changes in the dried residue, the amount of ash, and the total nitrogen were not uniform. In some patients there was a pronounced increase, while in others no change or a decrease was noted. Pick and Wasicky⁷ attributed the expectorant action of ipecac to the fact that it is capable of relaxing the smooth muscles of the bronchi. A variable degree of bronchospasm is elicited by infections of the lower respiratory tract. This spasm interferes with normal bronchial peristalsis. The relaxing influence of ipecac on the bronchial smooth muscles improves their functional capacity. Luisada⁸ demonstrated that electrobronchographic tracings are exaggerated after the administration of emetine, an alkaloid of ipecac. Ipecac is indicated in acute and subacute infections of the tracheobronchial system. The most practical way of prescribing it is in the form of syrup of ipecac.

The inhalation of steam has been a widely used popular method for centuries for the treatment of severe forms of acute bronchitis, laryngotracheobronchitis, and bronchiolitis. Its popularity is well justified on the basis of studies that revealed that it actually stimulates the secretory function of the bronchial mucosa and also that it stimulates the cilia.

Basch, Holinger, and Poncher⁷ carried out an important clinical investigation concerning the effect of the inhalation of steam or moisture on the physical and chemical properties of sputum. Specimens were secured by carefully observed postural drainage or by bronchoscopic suction. They noted that after steam inhalation the viscosity of the sputum was greatly lowered and that the dried residue and the total nitrogen content of the specimens examined were markedly reduced.

Inhalation of volatile oils (menthol, thymol, oil of eucalyptus, oil of turpentine) is followed by increase in the secretions of the glands of the bronchial mucosa. Also, volatile oils stimulate bronchial peristalsis and ciliary motion.

4. Perry, W. F., and Boyd, E. M.: A Method for Studying Expectorant Action in Animals by Direct Measurement of the Output of Respiratory Tract Fluids, *J. Pharmacol. & Exper. Therap.* 73: 65, 1941.

5. Basch, F. P.; Holinger, P., and Poncher, H. G.: Physical and Chemical Properties of Sputum; Factors Determining Variations in Portions from Different Parts of Tracheobronchial Tree, *Am. J. Dis. Child.* 62: 981, 1941.

6. Tuft, L., and Levin, M. N.: Studies of the Expectorant Action of Iodides, *Am. J. M. Sc.* 203: 717, 1942.

7. Pick, E. P., and Wasicky, R.: Zur pharmakologischen Analyse des Emetins. *Arch. f. exper. Path. u. Pharmacol.* 80: 147, 1916-17

On the basis of the pioneering observations of Henderson,⁸ I have been administering carbon dioxide as an expectorant since 1930.⁹ Its administration is a simple and safe procedure and does not interfere with the comfort of the patient. In my experience it has proved to be the most efficient expectorant. The benefits derived from its use are noticeable subjectively and objectively: 1. Spells of strenuous, exhausting coughing are prevented, and rest is thereby secured for the patients and particularly for the lungs. 2. An unproductive cough is transformed into a useful one. 3. Directly after inhalation, the amount of expectorated sputum is increased and its character changes from a heavy, thick, and tenacious type into a thinner, serous, and more watery kind. 4. The use of expectorant drugs and narcotics can be reduced.

The effectiveness of carbon dioxide is attributable mainly to the following factors: 1. It is a powerful respiratory stimulant and induces increased inspiratory movements of the diaphragm and the chest wall that, in turn, cause a stretching and dilatation of the bronchial tubes. 2. It stimulates the myoelectric structures of the lung and leads to a forceful peristaltic movement of the bronchi. 3. It liquefies mucopurulent inflammatory exudate that stagnates in the bronchial tract.

The apparatus used in my work consists of a tank, containing a mixture of 5% carbon dioxide and 95% oxygen, mounted on a small platform on casters. A reducing valve and flow-meter are attached to the tank. A BLB (Boothby-Lovelace-Bulbulian) mask or OEM (Oxygen Equipment Manufacturing Company) mask can be used for the administration of the gas mixture. The meter is set to a flow of 5 liters per minute. The

inhalations are administered three times a day, or more often if needed.

The mixture of 5% carbon dioxide and 95% oxygen can be used as a vehicle for the inhalation of aerosolized solutions of antibiotics (penicillin, streptomycin, and others).

I prefer the use of aerosolized antibiotics after satisfactory evacuation of the lung following carbon dioxide-oxygen inhalations. In this manner, it is more likely that the antibiotics inhaled gain a direct access to and contact with diseased areas.

Contraindications to carbon dioxide inhalations are (1) pulmonary hemorrhage, (2) acute pleurisy, (3) pronounced hypertension, and (4) extrapulmonary causation of cough.

CONCLUSIONS

1. The selection of remedies for the management of cough should be determined on the basis of pulmonary findings as well as the patient's general condition.

2. So-called expectorant drugs not only facilitate expectoration but also accelerate resorption of inflammatory exudate. This combined effect may be designated as bronchocatharsis.

3. Even the most efficient management of cough does not absolve the physician of the responsibility of treating the underlying disease on an etiologic basis.

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9. Banyai, A. L.: Carbon Dioxide Inhalation in Pulmonary Tuberculosis, *Am. Rev. Tuberc.* **30**: 642, 1934; *Dis. of Chest* **4**: 8, 1938; *Modern Treatment of Cough*, Hoja tisiol. **7**: 159, 1947.

EARLY DIAGNOSIS IN MASSIVE GASTROINTESTINAL HEMORRHAGE

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In the past, extensive efforts to achieve early diagnosis of the cause of massive upper gastrointestinal hemorrhage were limited by the fear of exacerbation of bleeding. In recent years, the wider use of prompt surgical intervention has been made possible by advances in surgical techniques, improved understanding of transfusion, and the greater availability of blood for this purpose. Since patients requiring emergency surgery must be differentiated promptly from those who should be treated without operation, the need for early accurate diagnosis of the cause of bleeding has been intensified. Diagnosis based on clinical grounds alone has proved unreliable in many instances; accordingly, we have employed adjuncts

to early diagnosis during the past three years at the Boston City Hospital. Emergency roentgen examination of the upper gastrointestinal tract was performed on almost all the patients studied. In order to help differentiate patients with operable lesions such as peptic ulcer from those with esophageal varices, the sulfobromophthalein retention liver function test was employed as a screening test for cirrhosis of the liver. Patients with retention indicating serious liver disease were further examined for the presence of esophageal varices by various methods, including emergency esophagoscopy, esophageal balloon tamponade, and roentgenography. The purpose of this paper is to review the usefulness and limitations of this early and complete diagnostic regimen.

EARLY ROENTGEN EXAMINATION

Patients with massive gastrointestinal hemorrhage were admitted to the medical wards. The admitting physician evaluated the severity of the bleeding and instituted replacement therapy. Emergency roentgen examination¹ of the upper gastrointestinal tract was routinely sched-

The late Dr. Franklin W. White and Dr. Stephen Maddock assisted in this study.

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From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard) and the Department of Roentgenology, Boston City Hospital, and the Departments of Medicine and Roentgenology, Harvard Medical School.

uled for the following morning. All food and oral medication were omitted for a period of 8 to 12 hours prior to the x-ray studies. Of 123 patients x-rayed, 74 were examined within 48 hours and 19 others within 72 hours after admission. All but six patients were examined within the first week. The examination was postponed when active bleeding or definite shock was present on the morning of the scheduled examination. Some of the patients were unable to cooperate because of hepatic stupor or incipient delirium tremens. When delayed for any reason, the procedure was rescheduled for the following morning. The extent of the studies depended on the patient's condition and was decided by the roentgenologist in consultation with the ward physician. Complete roentgen examinations, including fluoroscopy, multiple spot roentgenograms, and routine roentgenograms, were accomplished on 106 patients. Pressure cone studies were included in 59 instances. Of the remaining 17 patients, 13 were examined in the recumbent position only. The examinations of four patients were considered unsatisfactory because the studies were incomplete.

The findings at the initial roentgen examinations were compared with subsequent roentgen, gastroscopic, and esophagoscopy examinations and with observations made at 29 operations and six autopsies. Peptic ulcer was diagnosed 91 times, (65 duodenal and 26 gastric), esophageal varices 5 times, gastric cancer 3 times, gastritis 40 times, and marginal ulcer twice. Fifty-three patients had multiple lesions. No satisfactory final diagnosis was made on 12 patients, 10 of whom could not be studied adequately. The initial roentgen diagnosis was confirmed in 92 cases. A lack of correlation between the initial roentgen examination and all subsequent diagnostic procedures was noted in 14 patients. The diagnoses involved included peptic ulcers in 5 patients, esophageal varices in 2, and gastritis in 7. Only three of these 14 were completely examined initially. Although the exact diagnosis was not made at the initial examination of the 14, useful information was regularly obtained. When the roentgen examination was repeated in a more thorough manner two or three days later, it yielded the correct diagnosis in most instances. Seven ulcers (5 gastric and 2 duodenal) clearly defined on the initial roentgen examination healed so rapidly that they would not have been demonstrable had the initial roentgen examination been unduly delayed. The accurate localization of lesions of the upper gastrointestinal tract expedited the decision regarding operation and eliminated the necessity for time-consuming exploratory procedures in those patients who required operation.

In 111 of the 123 cases there was no evidence of renewed or continued bleeding after roentgen studies. In 12 patients who did bleed severely after returning from the x-ray room, it was not possible to establish or disprove a causal relation between the roentgen procedure and the subsequent bleeding. No deaths could be attributed to the emergency roentgen examination.

These studies indicate that emergency roentgen examination of the gastrointestinal tract can be performed with a high degree of accuracy and that more extensive examinations can be carried out with greater safety than was

formerly believed possible. The use of early roentgen re-examination is recommended as a valuable adjunct to the initial study when necessary. Emergency roentgen examination of the gastrointestinal tract proved indispensable for the early correct diagnosis of the cause of hemorrhage in many instances.

DIAGNOSIS OF ESOPHAGEAL VARICES

Surgical intervention is contraindicated during active bleeding from esophageal varices in patients with cirrhosis of the liver. These patients must be differentiated promptly from patients who may require surgery. Clinical recognition of liver disease of sufficient severity to cause varices is not always possible, especially in the absence of jaundice. A simple test of liver function, therefore, was sought to help screen out patients with cirrhosis.

Sulfobromophthalein Sodium Retention Test.—The sulfobromophthalein sodium retention liver function test² proved to be a rapid, safe, and reliable means for accomplishing this purpose when the test was performed during active bleeding soon after the patient was admitted to the hospital. Five milligrams of dye per kilogram of body weight was injected intravenously, and the retention in the blood was determined at the end of 45 minutes.³ In a group of more than 61 patients² the following observations were made: Normal sulfobromophthalein retention (5% or less) excluded the possibility of liver disease severe enough to cause esophageal varices. A high retention (15% or greater) indicated the possibility of serious liver disease, and immediate measures were taken to examine the esophagus for the presence of varices, especially when the decision to operate depended on the findings. Liver disease of lesser severity than cirrhosis was also accompanied by initially high retention, which dropped within a day or two to only slightly elevated or normal levels, differing from results in those with cirrhosis, who had persistently high retention. Although severe shock, advanced age, and possibly fever could increase the sulfobromophthalein retention, the usefulness of the test was not impaired.⁴ Varices caused by extrahepatic portal obstruction (Banti's syndrome) are not distinguished by the test in the absence of cirrhosis. Clinical recognition of this condition must be relied on (youth, splenomegaly, associated diseases). We have seen no examples of this condition during the present study.

Although roentgen demonstration of esophageal varices in cooperative, nonbleeding patients is usually suc-

1. Drs. Simon R. Hershorn and Thomas P. Cotter actively participated in the roentgen studies, more detailed presentation of which may be found in Zamcheck, N.; Cotter, T. P.; Hershorn, S. E.; Chalmers, T. C.; Ritvo, M., and White, F. W.: Early Roentgen Diagnosis in Massive Bleeding from the Upper Gastro-Intestinal Tract: Clinical Evaluation of Safety and Reliability of the Method in 123 Patients, *Am. J. Med.*, to be published; and Ritvo, M.; Cotter, T. P., and Zamcheck, N.: Early Roentgen Diagnosis in Massive Gastro-Intestinal Hemorrhage: II. Roentgen Aspects, *Am. J. Roentgenol.* 66: 728, 1951.

2. Zamcheck, N.; Chalmers, T. C.; White, F. W., and Davidson, C. S.: The Bromsulphalein Test in the Early Diagnosis of Liver Disease in Gross Upper Gastro-Intestinal Hemorrhage, *Gastroenterology* 14: 343, 1950.

3. It has been our experience that the use of the comparator block technique for the estimation of the sulfobromophthalein retention is not sufficiently reliable for this test, and the use of photoelectric colorimetry is recommended.

4. Since it is well known that some patients with proved cirrhosis may have normal or only slightly elevated sulfobromophthalein values when their liver disease is well controlled, it should be emphasized that the values given above are those obtained during or shortly after massive hemorrhage.

cessful, patients with active or recent hemorrhage may be too ill for transfer to the x-ray examining room or for complete roentgen examination of the esophagus. In such instances emergency esophagoscopy has proved to be the diagnostic procedure of choice.

Emergency Esophagoscopy.—When patients were too ill for roentgen examination, emergency bedside esophagoscopy⁵ was performed under topical anesthesia. Esophagoscopy performed in the operating room under general anesthesia was reserved for patients failing to cooperate under local anesthesia. During the past three years, diagnostic esophagoscopy has been performed on bleeding patients more than 50 times.⁶

In spite of the advanced age and severe illness of some of the patients, relatively little discomfort was encountered, and there were no deaths or serious complications from the procedure. It cannot be overemphasized, however, that esophagoscopy is a potentially dangerous maneuver, which demands experienced workers and trained assistants. Bedside examination should be discontinued if the patient fails to cooperate at any time. Esophagoscopy provides the only nonoperative method for the direct visualization of esophageal varices. Only by such direct visualization can it be established with certainty that the bleeding arises from varices rather than from a coexisting lesion, such as gastritis or peptic ulcer. When bleeding varices are found, oxycel gauze (absorbable hemostatic) may be introduced through the esophagoscope, with the aim of promoting clot formation, or esophageal balloon tamponade may be employed.

Esophageal Balloon Tamponade.—The difficulty of diagnosis as well as of management of bleeding esophageal varices has stimulated investigation of the use of esophageal balloon tamponade.^{6b} Preliminary observations with the triple lumen tube devised by Sengstaken and Blakemore⁷ have been made in approximately 20 patients at the Boston City Hospital. A sausage-shaped balloon mounted around a tube is introduced into the esophagus and, on inflation, compresses the esophageal veins; it is held in place by an attached second balloon, inflated in the cardiac end of the stomach. Separate lumens supply the two balloons, and a third permits liquid feeding and aspiration of stomach contents while the two balloons are in position. The prompt cessation of bleeding on introduction and inflation of the balloons and the resumption of bleeding on deflation supports the diagnosis of esophageal varices. Studies of the use of balloon tamponade are still preliminary, and at the present time we consider it desirable to use this procedure as a therapeutic method only when the diagnosis of esophageal varices has been clearly established. The in-

roduction of the tube into the esophagus is sometimes difficult because of its large caliber, and its prolonged use not only is troublesome but may be hazardous. Painstaking care by both physicians and nurses is necessary. Liquids may be introduced into the wrong one of the three tube openings and complicate the problem of tube withdrawal. Secretions, accumulating in the esophagus, present the hazard of aspiration. Despite these and other problems, esophageal balloon tamponade offers at present the most promising means for the immediate management of esophageal hemorrhage. Potentially, the tube enables diagnostic discrimination between multiple lesions of the upper gastrointestinal tract. For example, in two of our patients, coexisting esophageal varices and duodenal ulcers were diagnosed. The correct site of bleeding was indicated by appropriate observations made with the tube in place.

HEMORRHAGIC DIATHESSES

The above procedures supplement the routine history and physical and laboratory examinations by which medical causes of bleeding may be recognized. Generalized bleeding tendencies, as in drug intoxication, thrombocytopenia, uremia, and diseases of the spleen and bone marrow, are responsible for relatively few cases of massive gastrointestinal hemorrhage. When it does occur, clinical evidence of bleeding elsewhere usually accompanies the digestive tract bleeding. In one year gastrointestinal hemorrhage occurred in two known hemophiliacs in this clinic.

Severe liver disease, however, is regularly accompanied by multiple coagulation defects, which may contribute to bleeding from varices, ulcers, or gastritis in cirrhotic patients. Thus, 24 consecutive patients with advanced cirrhosis and massive gastrointestinal bleeding all manifested laboratory evidence of defective coagulation.⁸ Twenty-two of these patients had demonstrable lesions of the upper digestive tract; the remaining two had none. Only 2 of these 24 patients had clinical evidence of a generalized bleeding defect, i. e., purpura, diffuse petechiae, or multiple bleeding sites.

Simple screening laboratory procedures are usually sufficient to reveal the blood dyscrasia: examination of stained smear for thrombocytes, determination of bleeding and clotting times, tourniquet test, and one-stage prothrombin determination will identify most cases.⁹

COMMENT

Effective application of early and complete diagnostic studies is dependent on the collaboration of physicians conversant with the techniques described as well as on the availability of adequate laboratory and blood bank facilities. To the extent that these considerations are fulfilled or unsatisfied the dynamic approach to early diagnosis of patients with massive hemorrhage is justified or limited. In a large municipal hospital, where the incidence of liver disease is high and massive gastrointestinal hemorrhage is commonly the first manifestation of gastrointestinal disease, greater reliance must be placed on this energetic diagnostic regimen than may be required elsewhere. Management of a patient with serious hemorrhage without the benefit of exact diagnosis entails a definite

5. (a) Carter, M. G., and Zamcheck, N.: Esophagoscopy in Upper Gastrointestinal Bleeding, *New England J. Med.* 242: 280, 1950. (b) Desforges, G., and Aves, F. H.: The Diagnosis of the Cause of Massive Bleeding from the Esophagus, to be published.

6. The application of esophagoscopy to this problem during this study was initiated by Dr. Max Carter of the Thoracic Surgical Service and continued by other resident members, including Drs. Axel Kyllonen, William Sieber, George Ware, Frederick Aves, and Gerard Desforges.

7. Sengstaken, R. W., and Blakemore, A. H.: Balloon Tamponade for the Control of Hemorrhage from Esophageal Varices, *Ann. Surg.* 131: 781, 1950.

8. Studies are being conducted by Dr. Jane Desforges of the Thorndike Memorial Laboratory.

9. Frommeyer, W. B., and Epstein, R. D.: Medical Progress: Hemorrhagic Diseases, *New England J. Med.* 241: 700 and 743, 1949.

risk, which may often exceed the potential dangers of the diagnostic procedures.

Abundant justification for the application of prompt and complete studies was found in a review of 101 unselected fatal cases of massive gastrointestinal hemorrhage obtained from all services at the Boston City Hospital and studied post mortem at the Mallory Institute of Pathology between 1945 and 1949.¹⁰ One-third of the patients had died within 24 hours of hospitalization, more than half within three days, and approximately two-thirds within one week. Since, in the fatal cases, one-third of the patients had bled from varices and approximately one-half from peptic ulcers, the need for the prompt differentiation of these two groups was further emphasized. The same study pointed out that laboratory aids to the diagnosis of massive gastrointestinal hemorrhage are not a substitute for clinical awareness. In 29 cases, the existence of hemorrhage was obscured by the presence of other major clinical disorders and was totally unsuspected when the patients were first admitted to the ward. The existence of massive gastrointestinal hemorrhage was first disclosed at autopsy in nine cases; five of the patients had been hospitalized for less than four days. It is surprising that 32 fatal episodes of bleeding were initiated after the patients were hospitalized for other conditions and hemorrhage was unsuspected until autopsy in 15 of these. Roentgen examination of the gastrointestinal tract was performed on only 12 of these patients, and in none prior to the sixth hospital day.

Despite the most careful efforts, a diagnosis cannot be established in some cases until operation. Some patients bleed so massively on arrival at the hospital that they are sent promptly to the operating room after nonsurgical causes of bleeding and hepatic cirrhosis have been excluded. A few may arrive at the operating room with erroneous diagnoses. The responsibility for accurately finding the cause of bleeding then falls on the surgeon. Certain lesions of the upper gastrointestinal tract that cannot always be diagnosed preoperatively may be readily identified at operation. These include acute superficial ulcers of the duodenum and the stomach, marginal ulcers, acute gastritis, duodenitis, and submucosal aneurysms. For this reason, in massive persistent bleeding operation should not be unduly delayed when no clear-cut diagnosis has been achieved and nonsurgical causes of bleeding have been excluded.

At laparotomy, careful inspection should be made of all organs for deformity, color and blood vessel changes, local edema, and abnormality of regional lymph nodes and lymphatic drainage areas. The small bowel should be transilluminated. Gastrotomy, duodenotomy, or both are essential when the site of the lesion cannot be found after preliminary inspection and palpation. Trauma to mucosal surfaces, which may obscure the significant pre-existing mucosal lesions, must be avoided. Although the duodenal cap may appear normal on external inspection and feel normal when palpated through a gastrotomy incision, acute shallow ulcerations may be seen when it is inverted through the pylorus. Similar lesions may be seen in the cardiac portion of the stomach and at gastroenterostomy stomas.

Although the number of cases in which the condition is undiagnosed at operation are reduced by this complete examination, there remain a few patients bleeding from lesions that cannot be found. The critical state of some may preclude time-consuming, painstaking exploration. View of the bleeding site may be obstructed by immovable organs, blood, or tenacious mucus. Some lesions are difficult to find even with the extirpated stomach in hand. Since most upper gastrointestinal bleeding occurs from lesions located in the lower two-thirds of the stomach and the proximal 4 to 6 cm. of the duodenum, resection of these segments may be life-saving in such instances.

In the past, the difficulty of achieving a rational selection of patients requiring emergency surgery for massive bleeding yielded inevitable errors and sometimes resulted in controversy between enthusiasts for "surgical" and those for "medical" treatment. It is hoped that the diagnostic regimen here described will facilitate individualized management of these patients.

SUMMARY

Prompt diagnosis of the cause of massive upper gastrointestinal hemorrhage may be facilitated by the usual history and physical and laboratory examinations, aided by emergency roentgen examination. The prompt recognition of patients bleeding from esophageal varices is expedited by use of the sulfobromophthalein sodium liver function test and esophagoscopy and balloon tamponade. Early diagnosis of the cause of bleeding expedites selection of patients requiring surgical intervention. Properly applied, this diagnostic regimen is advantageous for use at the large municipal hospital and may be of benefit wherever appropriate facilities and trained personnel are available.

10. Chalmers, T. C.; Zamcheck, N.; Curtis, G., and White, F. W.: Fatal Gastro-Intestinal Hemorrhage: A Clinicopathological Study, to be published.

Coronary Disease.—Complete occlusion or considerable narrowing of one or more coronary arteries may exist without giving rise to any clinical signs or symptoms and without having produced myocardial damage. The apparent inconsistency between the presence of long standing obstructive arterial lesions and the absence of significant pathologic or clinical evidence of myocardial damage is dispelled by the demonstration of a collateral circulation which serves as a bypass in relation to the obstruction in each of these hearts. . . . In . . . angina pectoris, coronary failure and acute myocardial infarction, the underlying mechanism seems to be a relative disproportion between the requirements of the heart for blood and the supply through the coronary arteries. The changes in the myocardium resulting from this disproportion depend solely on the extent and duration of the relative ischemia, not on the manner in which they are produced. The absolute necessity for immediate and complete bed rest, sedation, reduction of excessively high cardiac rates and other measures designed to reduce the work of the heart, in the presence of prolonged cardiac pain is emphasized as a means of limiting the extent of myocardial necrosis or even preventing its development. Such a regimen also affords an opportunity for the development of a more adequate collateral circulation. Similar considerations would seemingly apply to patients in whom angina pectoris suddenly appears or when the frequency or intensity of the attacks suddenly increases.—Herrman L. Blumgart, *Coronary Disease: Clinical-Pathologic Correlations and Physiology, Bulletin of the New York Academy of Medicine*, December, 1951.

PRESENT STATUS OF THERAPY IN MYASTHENIA GRAVIS

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The neuromuscular disorder known as myasthenia gravis was first described by Willis in the 17th century. The clinical features were more distinctly outlined by Erb in 1878, and the periods of remission were emphasized by Goldflam, so that the condition frequently has been referred to as Erb-Goldflam's disease. Since this article is designed to focus attention on the present status of therapy in myasthenia gravis, there will be no effort made to consider in detail the pathology and symptomatology of this disease. For a comprehensive survey of these aspects, reference may be made to the excellent review by Keschner and Strauss.¹

The chief clinical feature of myasthenia gravis is muscle fatigability on sustained effort. The initial symptoms most often appear in the extraocular muscles, producing ptosis and a variable diplopia. The extraocular

hood the disease appears to be commoner in the female. The course of illness in most cases is characterized by gradual onset and by remissions of variable duration—they may extend over a period of months or years. Occasionally the onset may be sudden, and an apparent post-traumatic onset has been observed. Monosymptomatic myasthenia has been noted usually in the form of unilateral ptosis, and one such case is included in the examples to be mentioned. Noteworthy is the fact that muscle weakness in myasthenia gravis will consist of an element of weakness that is more or less completely eliminated by rest and another element of weakness that appears to be persistent and relatively unaffected by rest. It is the latter element that becomes pronounced in those patients who are refractory to treatment and who succumb despite treatment.

Some discussion of the current concepts regarding the pathogenesis of myasthenia gravis is pertinent, since the major advances in the treatment of this disease have been attributable to and have reflected improvement in our understanding of the underlying pathophysiology. The pathogenesis of this disease remained obscure until the development of the theory of chemical mediation of nerve impulses at synaptic junctions. It was assumed that the nerve impulse was transmitted at the myoneural junction by the sudden liberation of acetylcholine, with this chemical reaction quantitatively controlled by the chemical counteraction of cholinesterase. My previous attempt to evaluate therapy in myasthenia gravis 10 years ago² was made when the favored concept about the pathogenesis of this disease consisted of the hypothesis that an abnormally rapid destruction of acetylcholine was a consequence of overactivity of cholinesterase. During the last decade this concept has been largely replaced by the hypothesis which emphasizes impaired synthesis of acetylcholine at the myoneural junction. In some respects this appears to be a more adequate explanation, but conclusive proof is lacking. The concept of a tendency towards curarization at the myoneural junction has also been postulated.

The obvious confusion which continues about the pathogenesis more or less accurately reflects the unsolved problems in the treatment of myasthenia gravis. Although a definitive concept is lacking with regard to the specific alteration in function at the myoneural junction, there has been increasingly favored the hypothesis of a basic metabolic or endocrine disturbance. Metabolic or endocrine dysfunction may be responsible for the development of myasthenia gravis through the production of a substance which possibly interferes with the synthesis of acetylcholine or possibly is curarizing in its action. It is now generally accepted that the liberation of acetylcholine is necessary in the transmission of nerve impulses at motor nerve endings. The assumption that inhibition of cholinesterase by neostigmine enables the action of acetylcholine to be prolonged at the myoneural junction has served as the basis for the administration of neostigmine



Fig. 1 (Eighth patient in Table 1).—(A) Myasthenic facies including complete bilateral external ophthalmoplegia; (B) patient's appearance eight years following spontaneous remission.

muscle involvement may be so severe as to produce a complete external ophthalmoplegia (Fig. 1A). Weaknesses of the facial muscles, muscles of mastication, palate, pharynx, and larynx are commonly observed manifestations. The characteristic myasthenic facies is due to disappearance of normal folds as well as a lack of compensatory furrowing of the forehead in the presence of ptosis. Pain in the neck may be an early symptom and is due to weakness of the neck muscles. In some instances weakness of the muscles of the extremities represents an early and prominent feature.

The disease usually occurs in young adults but has been observed at all ages. There are reports describing its appearance at birth, and I have observed the disease in an 81 year old man. During childhood and young adult-

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Read before the Section on Nervous and Mental Diseases at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 14, 1951.

1. Keschner, M., and Strauss, I.: Myasthenia Gravis, *Arch. Neurol. & Psychiat.* 17: 337 (March) 1927.

2. Schlezinger, N. S.: Evaluation of Therapy in Myasthenia Gravis, *Arch. Int. Med.* 65: 60 (Jan.) 1940.

in sufficient amounts to make transmission of the impulse more adequate in patients with myasthenia gravis.

Since the advent of neostigmine as a generally effective medicament in the treatment of myasthenia gravis,³ it has remained the accepted form of treatment in the vast majority of cases. It also has served as a basis for

years serves as a basis for reemphasizing the value of neostigmine. A representative group of cases, in which the patients were treated primarily with neostigmine and were observed over periods varying from 2 to 10 years, are outlined in Table 1. It is well known that most patients with myasthenia gravis tolerate neostigmine with

TABLE 1.—Patients Primarily Treated with Neostigmine and Ephedrine

Age	Sex	Symptoms	Course with Therapy
19	F	During 4 yr. diplopia and later ptosis; myasthenic facies; external ophthalmoparesis; myasthenia elicited in jaws and hands	Controlled with partial relief by 75 to 120 mg. neostigmine daily; partial remission during pregnancy; after 10 yr. medication limited to ephedrine
64	F	During 3 mo. diplopia and increasing ptosis; myasthenic facies; bilateral external ophthalmoplegia	Partial relief with 120 to 150 mg. neostigmine daily; death 4 yr. later due to coronary occlusion; (no ephedrine)
45	M	During 1 yr. diplopia and increasing ptosis; myasthenic facies; bilateral external ophthalmoparesis; palatal weakness	Diminishing benefit with 150 to 180 mg. neostigmine daily for 10 yr.
62	M	During 1 yr. neck pain followed by diplopia, dysphagia, dysarthria, and some generalized weakness; myasthenic facies; bilateral external ophthalmoparesis; myasthenia elicited in palate, tongue, and extremities	Excellent response initially to 120 mg. neostigmine daily; subsequent fluctuation slightly for 5 yr.
65	F	During 2 yr. diplopia and increasing ptosis; myasthenic facies; bilateral external ophthalmoplegia	Partial benefit with neostigmine averaging 160 mg. daily; requires crutch glasses; no evidence of progression for 3½ yr. (no ephedrine)
22	M	During 1 mo. diplopia followed by weakness of the jaws, left arm, and left leg; left ptosis and multiple extraocular muscle pareses; myasthenia elicited in left extremities	Adequate control with 90 mg. neostigmine daily; gradual improvement over period of 2 yr.; spontaneous complete remission with no medication during past 2 yr.
30	F	During 2 mo. slight left ptosis; myasthenic left ptosis	Controlled by 90 mg. neostigmine daily; no change for 3 yr.
57	M	During 3 mo. generalized fatigue followed by ptosis and diplopia; myasthenic facies; bilateral external ophthalmoplegia; myasthenia elicited in extremities	Gradual improvement with 90 mg. neostigmine daily; almost complete spontaneous remission within 6 mo.; no medication for past 8 yr.
83	M	During 2 yr. episode of diplopia and painful left eye followed by similar episode involving right eye plus weakness of arms and legs; myasthenic facies; multiple extraocular muscle pareses; myasthenia elicited in arms and legs	Partial relief with 150 mg. neostigmine daily; spontaneous partial remission 10 mo. later with neostigmine reduced to 45 mg. daily for 2 yr.; no medication during the past year with almost complete remission and 45 lb. (20.4 kg.) increase in weight
17	F	During 1 yr. diplopia, ptosis, and general fatigue; myasthenic facies; myasthenia elicited in arms and legs	Considerable benefit with 90 mg. neostigmine daily, but gradual increase in dosage required over period of 7 yr. to level of 180 mg. daily
24	F	During 10 mo. arm and leg weakness followed by ptosis and dysphagia; myasthenic facies; myasthenia elicited in arms and legs	Considerable benefit obtained with 90 to 120 mg. neostigmine daily for 5 yr.
32	M	During 9 mo. left ptosis and diplopia; myasthenic facies; left ptosis and multiple extraocular pareses; myasthenia elicited in arms	Adequate control obtained with variable dose of neostigmine (90 to 180 mg.) daily; fluctuant course for 7 yr.
35	M	During 4 mo. ptosis followed by generalized fatigue; myasthenic facies; slight ptosis bilaterally; myasthenia elicited in arms and legs	Partial benefit with variable dose of neostigmine (90 to 180 mg.) daily; fluctuant course for 7 yr.; considerably increased disability coinciding with marital incompatibility; death of obscure origin reported within past year
27	M	During 8 mo. dysphagia with 45 lb. weight loss; myasthenic facies with slight ptosis; marked palatal weakness	Partial relief with variable dose of neostigmine (60 to 180 mg.) daily for 2 yr.; exacerbation requiring 300 mg. neostigmine orally plus neostigmine parenterally before meals; partial remission with complete rest and subsidence of marital incompatibility; return to work and neostigmine reduced to 150 mg. daily during past year
50	M	During 6 mo. diplopia and right ptosis; right external ophthalmoparesis including right ptosis	Symptomatic relief with 120 mg. neostigmine daily for 3 mo.; complete remission with no medicament during past year (no ephedrine)
88	F	During 1 mo. leg weakness, ptosis, and diplopia; bilateral external ophthalmoparesis; myasthenia elicited in legs	Partial benefit with 120 mg. neostigmine daily; after 2 wk. progressive weakness with dysarthria and dysphagia requiring 1.5 mg. neostigmine parenterally every 2 hr.; nitrogen mustard given for 4 days with no appreciable change; death 1 mo. later despite 1.5 mg. per hour neostigmine parenterally
63	F	During 5 yr. generalized muscle fatigue; diplopia and dysphagia for 4 yr.; 25 lb. (11.3 kg.) weight loss; myasthenic facies; bilateral external ophthalmoparesis; myasthenia elicited in arms and legs	Moderate benefit with 150 mg. neostigmine daily for 9 mo.; 200 mg. methylthiouracil daily for 3 mo. with no change
6	F	During 2 yr. variable ptosis and diplopia; myasthenic facies; multiple extraocular muscle pareses	Adequately controlled with 60 to 120 mg. neostigmine daily for 3 yr.
7	F	During 3 yr. diplopia and increasing ptosis; myasthenic facies; multiple extraocular muscle pareses	Adequately controlled with 60 mg. neostigmine daily; later increased to 120 mg. daily; observed over a period of 9 yr.

the earlier and more accurate diagnosis of myasthenia gravis.⁴ Although this neuromuscular disorder must still be regarded as relatively uncommon, there has been increasing recognition of the disease and more widespread interest from a therapeutic standpoint.

Many reports by various authors have clearly demonstrated the wisdom of maintaining neostigmine as the drug of choice in any consideration of the treatment of myasthenia gravis. A survey of the 65 cases in which the patients were personally observed during the past 10

little or none of the unpleasant side reactions that may occur in the normal person. The dose of neostigmine must be individually determined and is given orally as neostigmine bromide. Ordinarily the effective single dose is 30 mg., and the doses must be spaced in such a way as to obtain the greatest beneficial effect when the need

3. Walker, M. B.: Case Showing Effect of Prostigmine on Myasthenia Gravis, *Proc. Roy. Soc. Med.* 28: 759, 1935.

4. Viets, H. R., and Schwab, R. S.: Prostigmin in the Diagnosis of Myasthenia Gravis, *New England J. Med.* 212: 1280, 1935.

is greatest, either in terms of physical exertion or nutritional requirements. In those patients in whom unpleasant side effects occur, such as nausea, abdominal pain, and diarrhea, the simultaneous administration of atropine will prevent these toxic symptoms without diminishing the therapeutic effectiveness of the neostigmine. When required, there must be no hesitation in administering frequent doses of neostigmine, either orally or parenterally, in order to maintain vital functions, such as respiration. Rarely a crisis may require the continuous intravenous administration of neostigmine in a dose of 1.5 mg. per hour.⁵

It has been stated that patients treated with neostigmine are less apt to experience spontaneous remissions. My experience would not lead me to subscribe to that viewpoint. It is true that most patients who have been

showed that ephedrine enhanced the value of neostigmine, although it was not nearly as dramatic in its beneficial effect. Therefore, combined ephedrine and neostigmine medication is recommended as the preferred way of treating the average patient with myasthenia gravis. Of course, in the presence of hypertensive cardiovascular disease ephedrine should not be used. When it is used, I have found it advisable to administer it in a dosage of 25 mg. (8 mg. in children) two or three times daily. Phenylephrine (neo-synephrine®) hydrochloride and amphetamine (benzedrine®) sulfate have failed to show any beneficial effect in myasthenia gravis. Ephedrine in addition to neostigmine has been given in the cases outlined in Table 1, unless otherwise indicated.

Potassium, undoubtedly, has a beneficial effect in myasthenia gravis,⁷ but the degree of improvement is

TABLE 2.—Patients Whose Treatment Included Thymectomy

Age	Sex	Symptoms	Preoperative Course	Postoperative Course
25	F	During 1 yr. generalized fatigue followed by neck pain, left ptosis, and dysarthria; myasthenic facies; left ptosis; myasthenia elicited in palate and extremities	Neostigmine for 15 mo. with partial remission (120 → 45 mg.); then exacerbation with dysarthria and dysphagia; relatively refractory to 255 mg. neostigmine daily	Thymoma weighing 24 gm. removed with death 3 days later due to pulmonary atelectasis
35	F	During 3 mo. neck pain and diplopia followed by ptosis and generalized weakness; myasthenic facies with left ptosis	Asymptomatic for 6 mo. with 120 mg. neostigmine daily; then relapse with dysphagia, dysarthria, and generalized weakness; during next year partial remission and then severe relapse requiring 360 mg. neostigmine daily	Persistent thymus removed; neostigmine parenterally before and after operation required in dosage of 1 mg. per hr.; death 24 hr. after operation due to pulmonary atelectasis
31	F	During 2 yr. dysarthria and dysphagia followed by weakness of arms; dysphonia and dysphagia; myasthenia elicited in bulbar muscles and extremities	Partial relief with neostigmine for 1 yr.; then exacerbation requiring neostigmine parenterally, 1 mg. every 2 hr.	Persistent thymus removed; neostigmine parenterally before and after operation required in dosage of 1 mg. per hr.; subsequent gradual improvement with no medication during past 2 yr.
58	F	During 6 mo. diplopia and alternating ptosis; then progressive leg and arm weakness, dysphagia, dysphonia, and dyspnea; myasthenic facies; bilateral external ophthalmoparesis; jaw, palate, and tongue weakness; unable to stand without support	Initial improvement with 150 mg. neostigmine daily; 3 wk. later neostigmine parenterally before meals; x-ray therapy to thymus (2,800 r); neostigmine increased to 300 mg. daily plus 1 mg. parenterally before meals	Persistent thymus removed; 1 mg. neostigmine parenterally per hr. during operation; death 6 hr. later due to pulmonary atelectasis
5	F	During 4 mo. left ptosis followed by right ptosis; myasthenic facies; bilateral external ophthalmoparesis	Partial benefit with 75 mg. neostigmine daily; x-ray therapy to thymus (600 r); after 18 mo. acute exacerbation with dyspnea, dysphagia, and generalized weakness requiring neostigmine parenterally and then 180 mg. daily orally	Persistent thymus removed; subsequently gradual reduction of neostigmine to 75 mg. daily; present status similar to that noted initially
35	F	During 5 yr. ptosis and diplopia followed by generalized weakness, dysphagia, and dysarthria; myasthenic facies; palatal weakness; myasthenia elicited in arms and legs	Partial benefit with gradually increasing neostigmine dosage to level of 240 mg. daily; nocturnal dyspnea more marked after 3 yr.	Persistent thymus removed; some increase in strength with gradual reduction of neostigmine to 150 mg. daily
53	M	During 1 mo. right ptosis and slight generalized weakness; right ptosis; myasthenia elicited in extremities	Rapidly progressive muscle weakness generally with dysphagia and dyspnea; neostigmine both orally and parenterally gradually less effective, with 1 mg. per hr. parenterally required within 4 mo.	Exploratory mediastinotomy revealed no evidence of thymus; death 10 hr. after operation

treated with neostigmine continue to require this medication and with its use are in a position to maintain a more active way of life than would otherwise be possible. However, partial remissions and considerable fluctuation in the quantitative requirements for neostigmine are observed in many cases. Several of my patients have experienced complete remissions (Table 1 and Fig. 1).

Ephedrine, which was shown to be effective in myasthenia gravis⁶ shortly before the discovery of neostigmine, has remained a valuable drug. My previous study²

always slight when compared with neostigmine. On the basis of my own personal experience, I do not believe that its routine use is justified because of the unpleasant aspects which accompany its use in the massive dosage required, namely, 30 to 40 gm. daily.

Tetraethylpyrophosphate (TEPP) has been reported⁸ as having a beneficial effect comparable in degree with that produced by neostigmine but considerably longer in duration. Since this drug is a powerful inhibitor of cholinesterase, its action is primarily beneficial through a prolongation of the action of acetylcholine. Tetraethylpyrophosphate is more toxic than neostigmine, and the dosage is difficult to adjust. Repeated doses of atropine are required to counteract the undesirable side effects. This drug may be used in combination with neostigmine. The range between optimum benefit and toxic effects is narrow, making therapeutic control difficult. I have had no personal experience with this drug, but I am not convinced that it is a significant advance in the treatment of myasthenia gravis.

5. Viets, H. R.: Myasthenia Gravis Treated with Large Doses of Neostigmine Methylsulfate, Intramuscularly and Intravenously, and with Neostigmine Bromide Orally, *Am. J. M. Sc.* 208: 701, 1944.

6. Edgeworth, H.: A Report of Progress on the Use of Ephedrine in a Case of Myasthenia Gravis, *J. A. M. A.* 94: 1136 (April 12) 1930.

7. Laurent, L. P. E., and Walther, W. W.: The Influence of Large Doses of Potassium Chloride on Myasthenia Gravis, *Lancet* 1: 1434, 1935.

8. Grob, D., and Harvey, A. M.: Observations on the Effects of Tetraethyl Pyrophosphate (TEPP) in Man, and on Its Use in the Treatment of Myasthenia Gravis, *Bull. Johns Hopkins Hosp.* 84: 532, 1949. DeJong, R. N.; Westerberg, M. R., and Lures, J. T.: The Clinical Use of Organic Phosphate Cholinesterase Inhibitors in the Treatment of Myasthenia Gravis, *Tr. Am. Neurol. A.* 74: 126, 1949.

end of 48 hours and continued for a variable period of time. Millikan and Eaton,²² using larger doses than the previous authors, obtained somewhat similar results in two cases but reported no definite improvement in three other cases. As shown in Table 4, my personal experience has been limited to four patients, one of whom received cortisone and showed no evidence of improvement, with possibly some aggravation of his ophthalmoplegic manifestations.

The three patients who received corticotropin therapy showed symptomatic relapse during the course of treatment, with decided improvement starting rather abruptly about 72 hours following the termination of treatment (Fig. 2 and 3). This improvement was characterized by a considerable reduction in the neostigmine requirement and a return of strength sufficient to enable two of these patients to leave the hospital and return to ordinary activity. However, in no instance was there a complete remission, and the myasthenic manifestations remained quite evident. One of these three patients suffered a severe relapse, which developed rapidly after an interval of three months. Another course of corticotropin therapy duplicated the initial result, except that the degree of improvement was not as pronounced. Multiple remissions after repeated courses of corticotropin therapy have been reported by Torda and Wolff.²³

SUMMARY AND CONCLUSIONS

Combined neostigmine and ephedrine medication remains the treatment of choice for most patients with myasthenia gravis. Potassium and guanidine show a relatively slight beneficial effect in comparison with neostigmine, and undesirable side effects limit their usefulness. Tetraethylpyrophosphate and octamethyl pyrophosphoramide show a maximum therapeutic effect approximating that of neostigmine but of longer duration, however, toxic reactions and difficulty in adjustment of optimum dose make their routine use impractical. Concurrence of

hyperthyroidism and myasthenia gravis should be treated medically, primarily by elimination of hyperthyroidism through use of methylthiouracil or radioactive iodine, which appear to favorably influence myasthenia gravis. Thymectomy should be reserved for patients with demonstrable thymomas and a few selected patients who appear to be inadequately controlled with neostigmine and are not benefited by corticotropin (ACTH) therapy. Corticotropin therapy results in relapse during the course of therapy with noteworthy partial remission within 72 hours following termination of therapy, but subsequent relapse may occur, and ultimate therapeutic benefit remains undetermined.

ADDENDUM

Since submission of this article for publication, seven additional cases of myasthenia gravis have been treated with corticotropin. All these patients have shown a favorable response according to the characteristic "rebound" pattern, but five in the entire group have shown evidence of relapse subsequently. The degree of improvement following repetition of corticotropin therapy in most instances did not equal the initial improvement. The second patient in Table 4 received a total of four courses of corticotropin therapy and died suddenly during an acute exacerbation of myasthenia gravis on Jan. 1, 1952. This patient's illness was complicated by a refractory depressive psychosis, and he represents the only fatality in the series of patients treated with corticotropin. It would appear advisable to refrain from the use of corticotropin in those patients with myasthenia gravis who show a tendency to relapse repeatedly after a relatively short interval of improvement.

255 S. 17th St.

22. Millikan, C. H., and Eaton, L. M.: Clinical Evaluation of ACTH and Cortisone in Myasthenia Gravis, *Neurology* 1: 145, 1951.

23. Torda, C., and Wolff, H. G.: The Effects of Administration of ACTH on Patients with Myasthenia Gravis, in Mote, J. R.: Proceedings of the Second Clinical ACTH Conference, Philadelphia, The Blakiston Company, 1951, vol. 2, p. 126.

IMPORTANCE OF LIFE STRESS IN COURSE AND MANAGEMENT OF DIABETES MELLITUS

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and

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Vagaries in the behavior of patients have long been recognized as important limiting factors in the satisfactory control of diabetes mellitus. Physicians are familiar with the fact that many adolescents omit use of their insulin, fail to sterilize their equipment, and "raid the ice-box"—especially after conflicts with their parents. It is equally well known that many of the more obese patients of all ages are unable to curb their appetites and that this constitutes a major obstacle to the dietary control of a large part of the diabetic population. In addition, it has been often suspected, but not adequately demonstrated, that changes in the course of diabetes may result not only from the failure of the patient to follow the treatment regimen, but also from the direct metabolic effect of life

stress. An increasing body of evidence now indicates that even when diabetic persons adhere strictly to their prescribed regimen, significant alterations in their metabolism do occur as part of their adaptation to people and events in their environment. Because of this the physician has found it necessary to concern himself more than ever with the personality of his patients and the events and situations in their lives.

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Dr. Edward Tolstoi made available the facilities of the Diabetic Clinic of the New York Hospital for this study and criticized and encouraged this work.

THEORETICAL CONSIDERATIONS

Energy requirements in man are ordinarily fulfilled by the combustion of fat, carbohydrate, and protein in a proportion which varies according to the type and amount of food ingested and the amount of work being done. For example, during starvation a much larger proportion of fat is consumed than during periods when carbohydrate is being eaten regularly. The ability to utilize glucose is temporarily impaired; the glucose tolerance curve becomes elevated and prolonged and assumes the characteristics of a "diabetic" curve. Increasing amounts of beta-hydroxybutyric acid and aceto-acetic acid appear in the blood and urine. These "ketone bodies," once thought to be poisonous waste products of impaired fat combustion, now are recognized as valuable metabolites, readily utilized by all tissues except the central nervous system. They are normally present in human blood, but in much smaller concentration than glucose (approximately 0.2 to 2.0 mg. per 100 cc., expressed as acetone recovered), and enter readily into the Krebs' cycle, the "final common path" of energy production in muscle. Accompanying these metabolic changes during early starvation there occurs a transient diuresis which is as yet unexplained.

Such changes are not confined to starvation alone. Many and varied physical stresses, such as exhausting exercise, exposure to x-rays, surgical operations, fractures of large bones, repeated vomiting, and major infections, are all known to cause ketonemia, ketonuria, and impairment of glucose tolerance in nondiabetic persons. In broad terms it may be said that any stress which leads to a diminution in the amount of carbohydrate and protein food available, or to a relatively great increase in demands for energy, will lead to an increase in the proportion of fat burned relative to carbohydrate. The preferential utilization of fat under such circumstances appears to serve a valuable purpose. Body stores of fat are present in relatively large amount. Carbohydrate stores, on the other hand, are limited to the amount of glycogen present in the liver. When exhausted they must be replenished largely at the expense of body protein. Since a continued supply of carbohydrate is necessary for the function of the central nervous system and since the maintenance of body structure is jeopardized by the utilization of body protein, the conservation of carbohydrate and the increased utilization of fat during stress seems to be an appropriate mode of adaptation.

1. Mirsky, I. A.: Emotional Hyperglycemia, *Proc. Central Soc. Clin. Research* 19: 74, 1946.

2. Meyer, A.; Bollmeier, L. N., and Alexander, F.: Correlation Between Emotions and Carbohydrate Metabolism in 2 Cases of Diabetes Mellitus, *Psychosom. Med.* 7: 335, 1945.

3. (a) Hinkle, L. E., Jr.; Evans, F. M., and Wolf, S.: Studies in Diabetes Mellitus: III. Life History of 3 Persons with Labile Diabetes, and Relation of Significant Experiences in Their Lives to the Onset and Course of the Disease, *Psychosom. Med.* 13: 160, 1951. (b) Hinkle, L. E., Jr.; Evans, F. M., and Wolf, S.: Studies in Diabetes Mellitus: IV. Life History of 3 Persons with Relatively Mild, Stable Diabetes, and Relation of Significant Experiences in Their Lives to the Onset and Course of the Disease, *ibid.* 13: 184, 1951. (c) Hinkle, L. E., Jr., and Wolf, S.: Studies in Diabetes Mellitus: Changes in Glucose, Ketone and Water Metabolism During Stress, *A. Res. Nerv. & Ment. Dis., Proc.* 29: 338, 1950.

4. (a) Hinkle, L. E., Jr.; Edwards, C. J., and Wolf, S.: The Occurrence of Diuresis in Humans in Stressful Situations, and Its Possible Relation to the Diuresis of Early Starvation, *J. Clin. Invest.* 30: 809, 1951. (b) Hinkle, L. E., Jr.; Conger, G. B., and Wolf, S.: Studies on Diabetes Mellitus: The Relation of Stressful Life Situations to the Concentration of Ketone Bodies in the Blood of Diabetic and Non-Diabetic Humans, *ibid.* 29: 754, 1950.

It is well known that physical stresses increase the insulin requirements of persons with diabetes mellitus. There has long been an impression that life situations which are stressful to the person because of their significance to him might also produce such metabolic disturbances. Cannon observed glycosuria in laboratory animals in association with fear or rage. More recently Mirsky¹ has shown that situations arousing anxiety may cause a rise in blood glucose of the diabetic, and Meyer, Bollmeier, and Alexander² have observed that diabetics in conflict situations may excrete an increased amount of glucose. Except for these observations, however, experimental evidence on this point has been meager.

EXPERIMENTAL STUDIES

Observations were made on a group of 64 diabetic subjects encountered in the course of routine attendance at a diabetic clinic. Ages ranged from 12 to 81, and all grades of severity of diabetes were included. With each one, by giving careful attention to his life history and personality structure, using direct and indirect methods described in detail elsewhere,³ we made an attempt to discover his prevailing attitudes (both conscious and unconscious) and the persons and relationships important to his emotional security. Special attention was directed toward the setting in which the first symptoms of diabetes occurred, and the circumstances surrounding exacerbations and remissions. The reactions of a group of healthy nondiabetic persons to life stress were studied simultaneously in a similar fashion.⁴

In long-term studies extending over three years, periods of exacerbation and remission were correlated with events and attitudes in the life situation. Interviews with the physician were usually of an hour's duration and took place at intervals of one to three weeks. Ultimately, the patients discussed freely all aspects of their personal lives and brought to the physician their husbands, parents, and children for interviews. In essence, the physician became a family confidant, but maintained his primary affiliation with the patient. Using the technics of modern investigative psychiatry, he was able to elicit much information not usually uncovered by a brief medical history. When it appeared that a certain personal conflict was connected with the variations in the diabetic state, the pertinence of this conflict was tested in a short-term experimental setting. On the morning after an overnight fast, under carefully controlled conditions of activity, posture, and fluid intake, serial determinations of the subject's blood glucose, ketones, eosinophils, and serum inorganic phosphate and of his urinary excretion of water, chlorides, glucose, and ketones were made. Diabetic subjects were given no insulin for 24 hours before the experiments. After suitable base line observations had been made, the suspected topic of conflict was abruptly and vigorously introduced into the discussion. The interview often aroused in the diabetic patient feelings toward the interviewer similar to those he felt toward the parent, spouse, or sibling around whom the conflict centered. After an hour or more of such discussion, the interview was terminated on a reassuring and supporting note, and an effort was made to restore the original relation between the patient and the physician. However, the interview hour was not necessarily the only hour in which the subjects

were under stress. Because laboratory procedures such as these may in themselves have threatening implications for some people, because subjects may themselves introduce a stressful stimulus into an intended control procedure through their own ruminations, and because attitudes and feelings once aroused cannot always be

During quiet resting the blood ketone and glucose concentrations and the rate of output of urine of nondiabetic subjects changed very little during a morning in which no food was eaten. However, with continued fasting, the glucose concentration slowly fell toward a level of about 40 to 50 mg. per 100 cc.,⁶ and the blood ketone concentration rose. At about the same time there often occurred a moderate diuresis as a part of the adaptive process. This reaction observed in the fasting nondiabetic human being is shown graphically in Figure 1.

A similar phenomenon produced by a stressful situation without starvation is shown in Figure 2. A nondiabetic woman, 42, became apprehensive during the first hour while she was "waiting quietly" for what to her was an unfamiliar and threatening laboratory procedure. During the hour of interview she remained apprehensive, and, in addition, she was made angry and sad by the manner in which the interviewer discussed

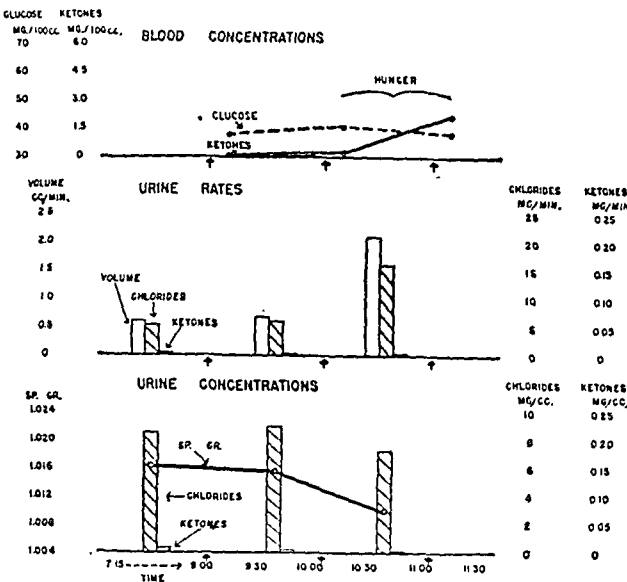


Fig. 1.—Rise in blood ketone concentration and diuresis occurring in a nondiabetic woman, 25, after 16 hours of fasting.

completely allayed in a brief period, some subjects were under stress during one or both of the hours other than the interview hours, as will be noted. The reactions of the subject to this procedure were evaluated not only by observing him carefully at the time, but also by a

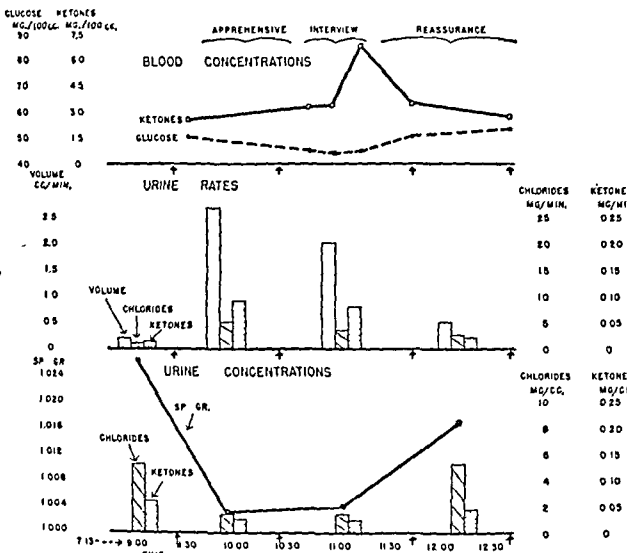


Fig. 2.—Fall in blood glucose, rise in blood ketones, and diuresis occurring in a nondiabetic woman, 42, during a stressful situation which aroused apprehension and anger.

review of his recollections and associations about the whole procedure.⁵ At a later date a similar study was carried out, with the interview centering around topics known to be more neutral or reassuring to the subject. In this manner more than 200 studies have been made on over 80 persons during a three-year period.

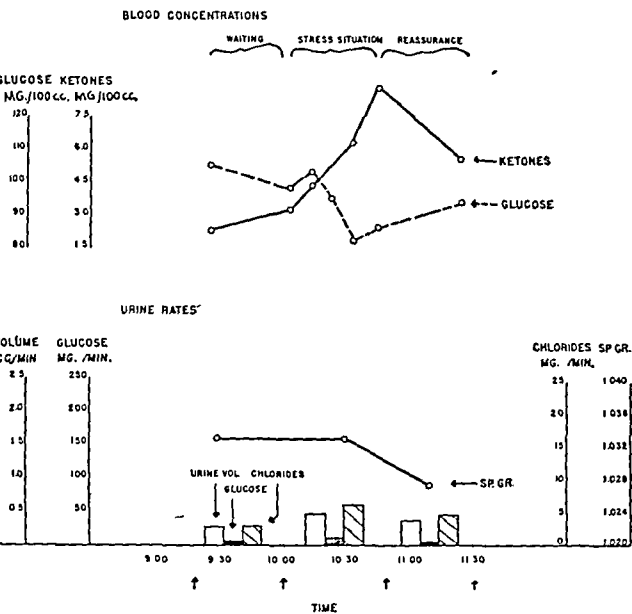


Fig. 3.—Rise in blood ketone concentration occurring in a diabetic woman, 55, taking 15 units of insulin daily, during a period of stress. This change was accompanied by a fall in blood glucose concentration without diuresis.

her conflict with her brother. During the third hour she regained her calm and good spirits when the physician changed his manner and guided the discussion to reassuring and diverting topics. It may be observed that a diuresis developed during the initial period of anxiety and that during the interview period, when the patient also began to feel angry and deprived, her blood ketone concentration rose steeply. Both the diuresis and the ketonemia subsided when the interview turned to more pleasant topics and the patient no longer felt threatened. It should not be inferred from this that the "emotions" were the cause of the metabolic changes but merely that the two types of change—"emotional" and "metabolic"—occurred at the same time as a part of the reaction of

5. Hinkle, Evans, and Wolf.^{2a} Hinkle, Evans, and Wolf.^{2b} Hinkle, Conger, and Wolf.^{4b}
6. Methods of blood glucose determination used in these studies largely exclude reducing substances other than glucose, and yield "normal" values of 50 to 80 mg. per 100 cc.

the subject to the stressful situation.⁷ It appears that certain types of emotional reactions often occur at the same time as certain physiological changes—for example, diuresis usually occurred in a setting of anxiety, and an increase in ketonemia usually occurred along with feelings of anger, dejection, and loneliness. Apparently an emotion and a bodily change may accompany each other regularly when both are what might be called “appropriate reactions” to the same stimulus—in this case the stimulus being that aspect of the situation which was interpreted by the subject as threatening.

Diabetic persons show a similar metabolic response to significant psychological stresses, but often it is much greater in magnitude. Figure 3 shows the steady rise in the blood ketones of an unemployed middle-aged seamstress, which occurred when the physician made her angry and dejected by detaining her in the laboratory

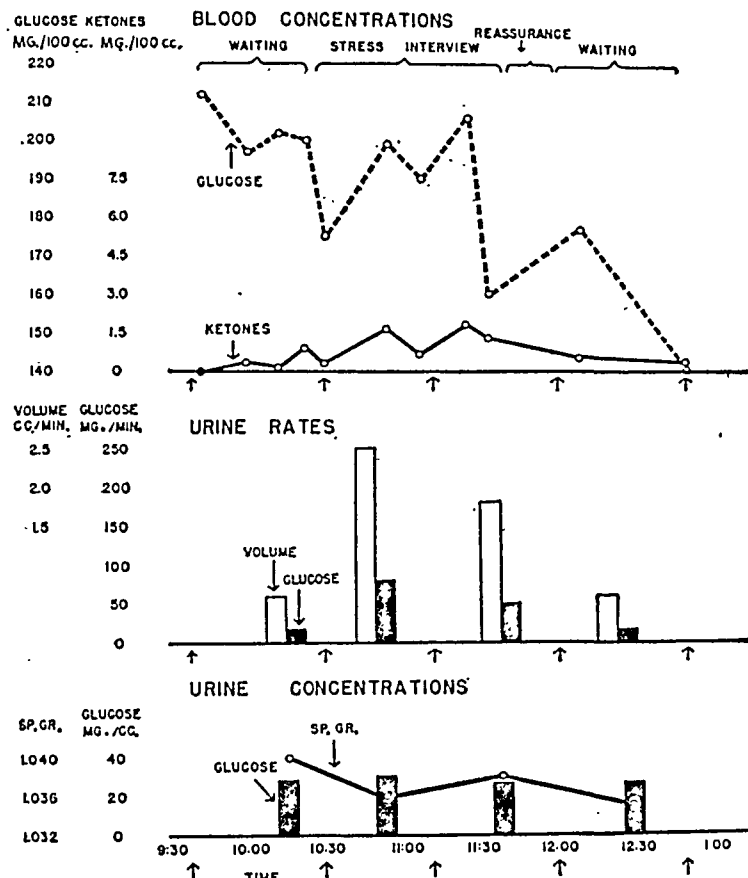


Fig. 4.—Diuresis occurring in a diabetic boy, 15, taking 50 units of insulin daily, who became anxious during a discussion of his conflict with his father. An increase in glucose excretion occurred despite the fall in blood glucose concentration.

at a time when she was expected to report for the first job she had been able to find for several months. The fluctuations of her fasting blood sugar are typical of diabetic persons under stress.

The patient in this study was not anxious, and no diuresis developed, despite the rise in her blood ketones. However, a “stress diuresis” associated with anxiety may be induced in diabetic persons regardless of whether or not they have glycosuria.⁷ Figure 4 shows the diuresis which occurred in a boy, 15, during a discussion of his conflict with his father. It may be observed that the rate at which he excreted sugar rose in parallel with the rate

at which he excreted water, despite the fact that his blood glucose concentration was falling throughout the entire period. On the other hand, during periods of relative relaxation and security diabetic persons sometimes have

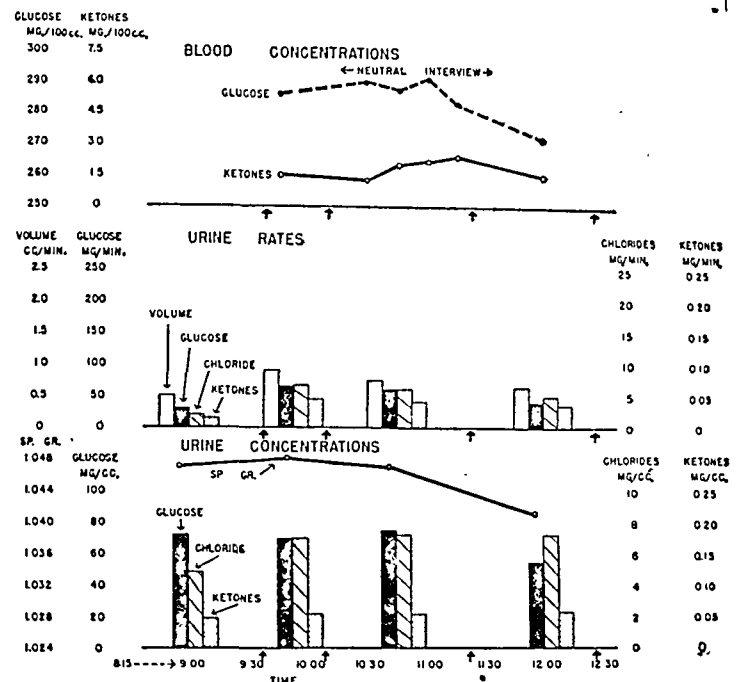


Fig. 5.—Diabetic boy described in Figure 4 exhibiting no polyuria and no symptoms of diabetes during a morning in which he felt relatively secure, relaxed, and diverted, despite the fact that his blood glucose concentration was 286 mg. per 100 cc., and his urine glucose concentration 7%. Blood glucose and ketone concentrations were relatively stable.

a relatively high blood sugar level, and a high concentration of glucose in their urine, without polyuria, thirst, or other symptoms. Figure 5 shows a control study on

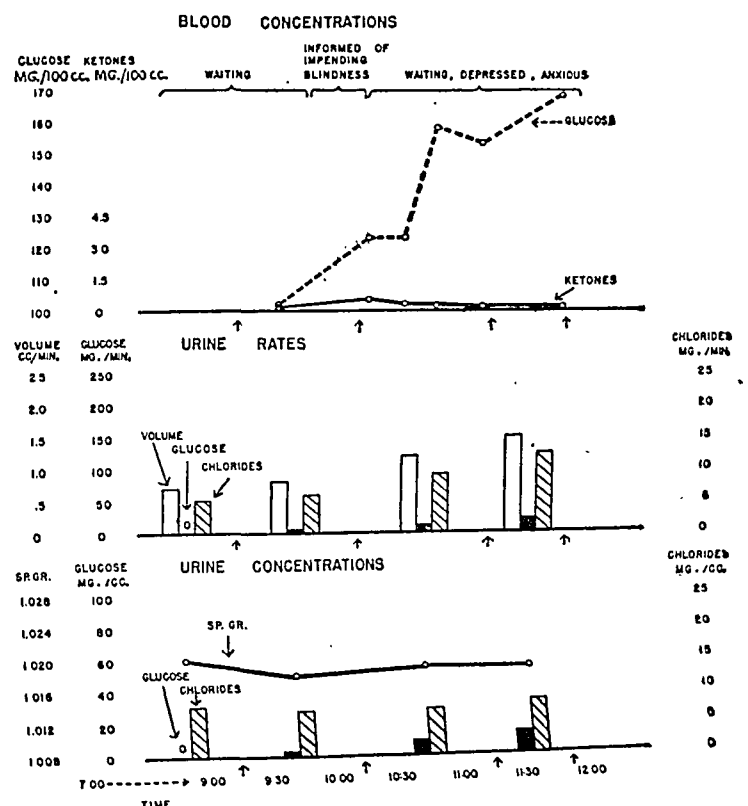


Fig. 6.—Glycosuria and rapid rise in blood glucose concentration in a diabetic man, 30, taking 30 units of insulin daily. He had just learned of his impending blindness.

the same boy, during a morning in which he felt relatively secure, relaxed, and diverted. Despite a blood glucose of 286 mg. per 100 cc. and a 7% glycosuria, he had no polyuria.

7. Hinkle, L. E., Jr.; Edwards, C. J., and Wolf, S.: Studies in Diabetes Mellitus: II. The Occurrence of a Diuresis in Diabetic Persons Exposed to Stressful Life Situations, with Experimental Observations on Its Relation to the Concentration of Glucose in Blood and Urine, *J. Clin. Invest.* 30: 518, 1951.

During the experiments illustrated in Figures 3 and 4 the fasting blood sugar level fell, but a rise in fasting blood sugar was observed under certain circumstances of stress. Figure 6 shows the rise in the blood sugar of a man, 30, with retinitis proliferans, which occurred after he learned that nothing could be done to prevent him from losing his vision. It may be observed that glycosuria developed also and that his rate of urine output rose from 0.7 to 1.5 cc. per minute.

The usual initial reaction of a fasting diabetic subject to a conflict situation of importance to him was a transient fall in his blood glucose level accompanied by a rise in ketonemia. If the stress was continued, the blood glucose ceased to fall, and might rise. In labile diabetics in the fasting state, the initial fall in blood sugar during periods of stress was sometimes large enough to precipitate hypoglycemic symptoms. On the other hand, in fasting persons suddenly made very fearful or angry, like the subject of Figure 6, a rapid rise in blood sugar, apparently as a result of epinephrine secretion, often

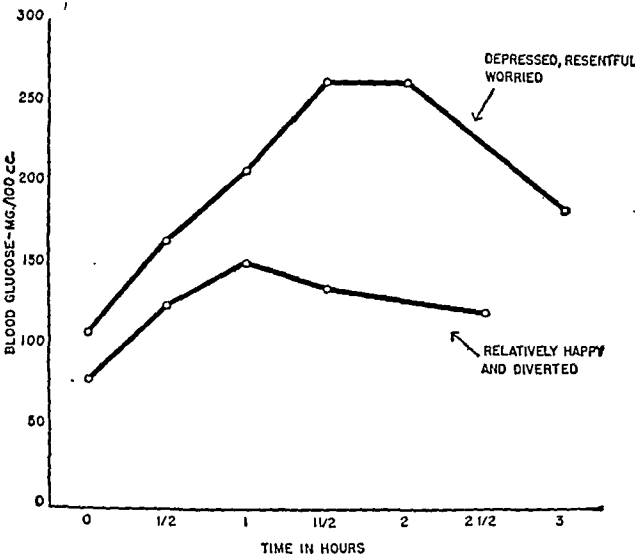


Fig. 7.—Changes in the shape of the oral glucose tolerance curve of a diabetic man, 47, occurring in association with changes in his mood and in his life situation. His diabetes was controlled by diet; he took no insulin.

developed. In addition to these effects on the fasting blood sugar, stress situations also affected the response of the patient to the ingestion of carbohydrate food. Situations associated with loneliness, sadness, and resentment were sometimes associated with a longer and higher ("more diabetic") glucose tolerance curve (Fig. 7); whereas, situations associated with less stress or with anxiety were associated with a flatter and less elevated curve.

When a diabetic person with a relatively high blood glucose level and an established glycosuria is placed in a conflict situation, his reaction to it may include a rapid rise in blood ketones and a greatly increased excretion of water, glucose, ketones, and chlorides (Fig. 8). In short-term experiments such as this we have observed a rise in blood ketones of 19 mg. per 100 cc. in 1 1/2 hours and the excretion of as much as 4.7 cc. of water per minute (282 cc. per hour), 490 mg. of glucose per minute (29.4 gm. per hour), and 25.2 mg. of chloride per minute (1.5 gm. per hour). In a setting of stress a

diabetic may excrete enough glucose to deplete his glycogen stores very rapidly (Fig. 9), and at the same time may lose large amounts of chloride and fixed base. Metabolic changes in diabetics in response to stressful

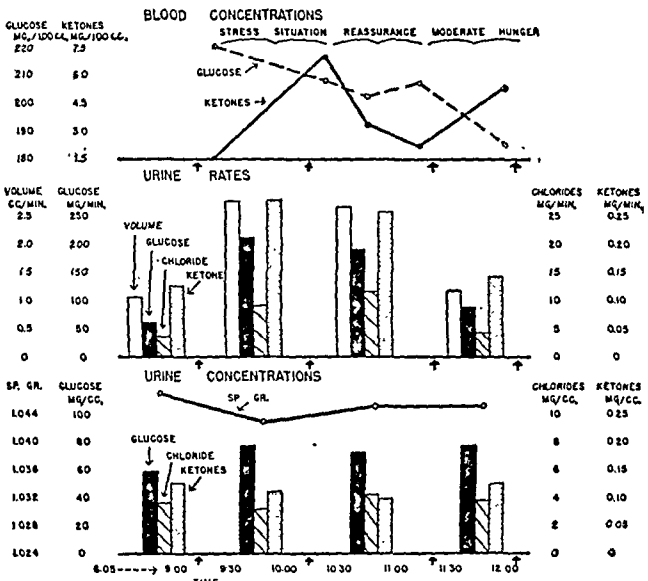


Fig. 8.—Effect of a stress situation on a diabetic subject (taking 90 units of insulin daily) in a borderline state of compensation showing rapid rise in blood ketones, associated with increased excretion of water, glucose, chlorides, and ketones.

life experiences may sometimes be of great magnitude, and they may have serious consequences if not promptly counteracted.

CLINICAL STUDIES

In the group of diabetic persons who were observed at intervals of one or two weeks for three years, it was found that major fluctuations in their symptoms and insulin requirements frequently coincided with important episodes in their lives. Figures 10 and 11 illustrate

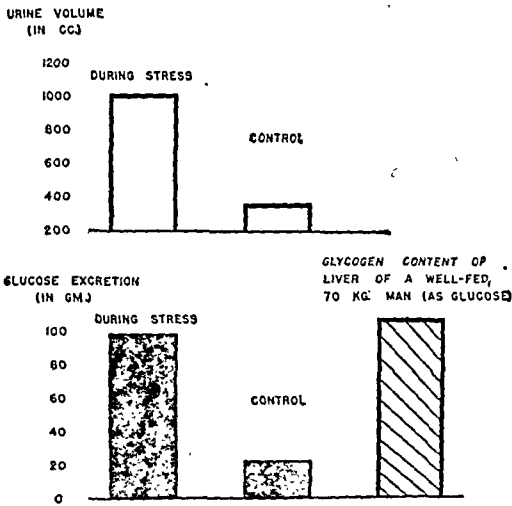


Fig. 9.—Magnitude of glucose and water loss during two comparable four-hour periods in a diabetic girl. Normally available stores of glycogen charted for comparison.

these findings in a girl, 15, who was followed by daily observations on her urine glucose and ketones, and of the events in her personal life.⁸ Although she had a constant glycosuria throughout the observation period,

ketonuria, thirst, and polyuria appeared only at times of acute conflicts with her mother. To make certain that these changes were not the result of her willful manipulation of her insulin intake, she was admitted to the hospital for further study. There, under carefully controlled conditions, she was again exposed to a conflict with her mother (Fig. 11). Thirst, polyuria, ketonuria, and dehydration promptly developed and continued for 48 hours. When the differences between the patient and her mother were reconciled, all the manifestations of ketosis disappeared, and the patient was restored to her former state of equilibrium, without use of additional insulin and without changes in fluid intake or diet.

Another patient, a girl, 14, on the hospital ward, was told that on the next morning she would have an operation which she thought was both dangerous and unnecessary. She became extremely anxious and resentful, and during the next 12 hours a ketonemia of 39.8 mg. per 100 cc. developed. Many instances of coma in association with life stress have been observed in persons outside the hospital.⁸

It was found that episodes of ketosis and coma very frequently occurred in a setting of interpersonal stress, although patients often concealed this fact from their physicians. The patients had responded to these conflict situations not only with direct physiological adaptations, but also with changes in their overt behavior which had repercussions on their metabolism. During periods of resentment, rebellion, and hopelessness, they might stop taking their insulin, eat a great deal of food (or stop eating entirely), or expose themselves to illness by such maneuvers as neglecting to sterilize their syringes. Life stress therefore led to ketosis by a variety of mechanisms, though it appeared that the direct metabolic response was the most important of these.

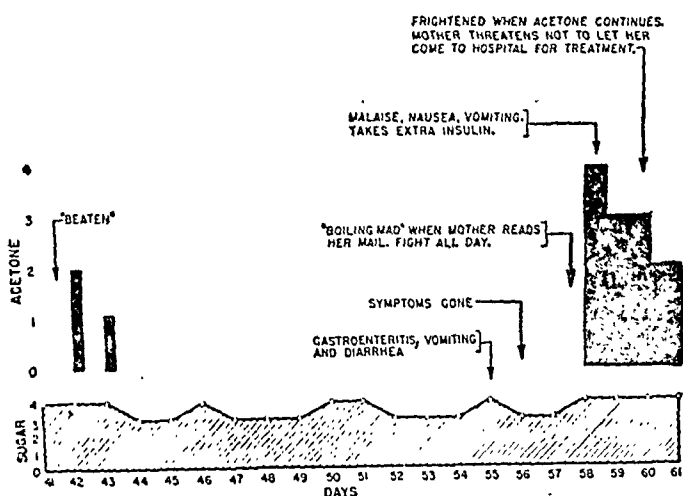


Fig. 10.—Observations on a diabetic girl, 15, showing temporal correlation between episodes of ketonuria and conflicts with her mother. These conflicts appeared to be a more potent cause of ketonuria than the episode of gastroenteritis which occurred on the 55th day.

Similar behavior patterns were observed so frequently in persons with diabetes that it seems unlikely that they could be explained on the basis of chance. For example, a very large percentage of the group had an extraordi-

nary appetite for food years before they had any clinical evidence of diabetes. They were persons who ate more when they felt tense, sad, lonely, or bored, because it made them feel calmer and more contented to do so. Sometimes they found this urge to eat almost uncontrollable. Because of it they had become fat. Because of it they found diabetic diets virtually intolerable. Because of it they "cheated," concealed their eating even

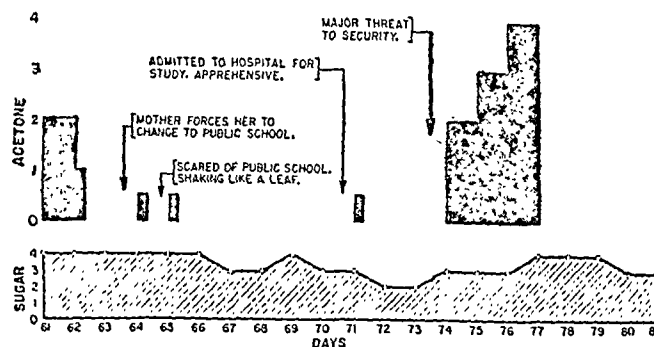


Fig. 11.—Further observations on subject of Figure 10 showing the episode of ketosis which occurred while she was in the hospital and which followed a conflict with her mother (74th day).

from themselves, felt ashamed, and tried to deceive their physician. Because of it adolescent diabetics found solace in the refrigerator or the candy store after an argument with their parents. Such behavior appeared to be almost as characteristic a symptom of diabetes as polyuria. It probably provides an explanation for the apparent paradox of the person who "eats himself into coma." For years physicians have observed that coma develops in patients "after an eating spree." This is such a common clinical phenomenon that the belief that overeating may cause ketosis has remained widespread long after the conclusive demonstration that carbohydrate food always has an antiketogenic effect.⁹ Apparently the diabetic person responds to stress with metabolic changes which lead to ketosis, and with an increased intake of food; the coincidence of these two responses has made it appear that the food intake is the cause of the metabolic change.

Other features of these diabetics' behavior and their life experiences which were seen with great regularity may be mentioned briefly. Even adults who had taken insulin for years admitted in confidence their intense dislike for insulin injections. Children and adolescents often detested them, and made the daily injection a painful ordeal for themselves and their parents. A large proportion of the patients had one parent (usually the parent of the same sex) whom they felt to be dominating and restrictive. Toward this parent they exhibited an unusual degree of both dependence and resentment. Periodic outbursts of anger and rebellion directed at this parent had been a feature of their behavior long before their diabetes developed. After the disease began these acute conflicts were accentuated, and were usually accompanied by exacerbations of the illness, including ketosis and coma. This was especially true in the adolescent group. The behavior of a large number of the adolescents was characterized by unreliability, unpredictability, and inability to learn by experience—features typically seen in persons with psychopathic personalities. In diabetics of all ages the onset of the symptoms of the disease usually took place in a setting of stress. Some-

8. Hinkle, L. E., Jr., and Wolf, S.: Experimental Study of Life Situations, Emotions, and the Occurrence of Acidosis in a Juvenile Diabetic, *Am. J. M. Sc.* 217: 130, 1949.

9. Mirsky, I. A.; Franzblau, A. N.; Nelson, N., and Nelson, W. E.: The Role of Excessive Carbohydrate Intake in the Etiology of Diabetic Coma, *J. Clin. Endocrinol.* 1: 307, 1941.

times this stress was a disease or injury, but more often it was related to the death of a parent, the loss of a husband, or a business reverse, and it was accompanied by feelings of anxiety, dejection, and deprivation. Such feelings often became chronic, and were associated with a feeling of inability to cope with the problems of life. Whether these psychological manifestations must be considered as an integral part of the total disease process which we call "diabetes mellitus" remains to be evaluated, but that they may have a most important effect on our efforts to manage the illness is clear from the available evidence.

COMMENT

Since the fasting blood sugar of labile diabetics may fluctuate rapidly and widely in response to the unpredictable experiences of their daily lives and since the blood sugar level of all diabetics seems to correlate only in the grossest manner with the presence or absence of thirst, polyuria, and ketonuria, it seems evident that random samples of fasting blood sugar provide a less reliable indication of the clinical state of the patient and (except in the detection of insulin reactions) are of less value as a guide to therapy than has been generally thought. For much the same reasons, the presence or absence of glucose in random samples of urine may not give a reliable indication of the clinical state of the patient. On the other hand, since thirst, polyuria, weight loss, and dehydration are direct functions of the volume of urine excreted, the 24-hour urine volume appears to be a relatively reliable indicator of the state of control of the disease. Diabetic persons without impaired kidney function whose urine volume lies between 1 and 2 liters a day maintain their weight and have no symptoms of diabetes. They may or may not have glucose in their urine, depending on the fluctuations in their food intake

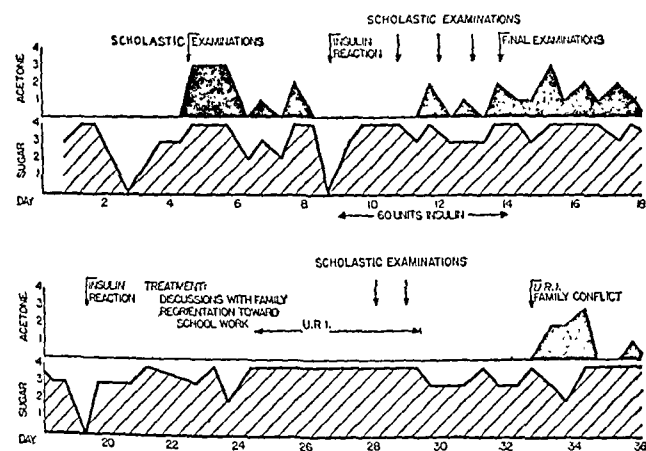


Fig. 12.—Observations on a girl, 15, showing temporal correlation between scholastic examinations (indicated by arrows) and the appearance of ketonuria. Daily dose of insulin was 70 units except when otherwise noted. U.R.I. = upper respiratory tract infection.

and blood sugar level during the day, but usually the number of grams of glucose which they excrete is small. Since ketonemia of moderate degree may occur in the absence of polyuria (Fig. 3) and since the qualitative tests for ketonuria respond to the concentration of ketone bodies in the urine rather than the total amount present, one occasionally sees nondiabetic as well as diabetic

persons with a normal urine volume and a positive nitroprusside test. Under these circumstances a "trace of acetone in the urine" does not have the significance which it has when it occurs in association with polyuria.

In similar manner, our therapeutic goals may have to be modified somewhat in the light of added knowledge.

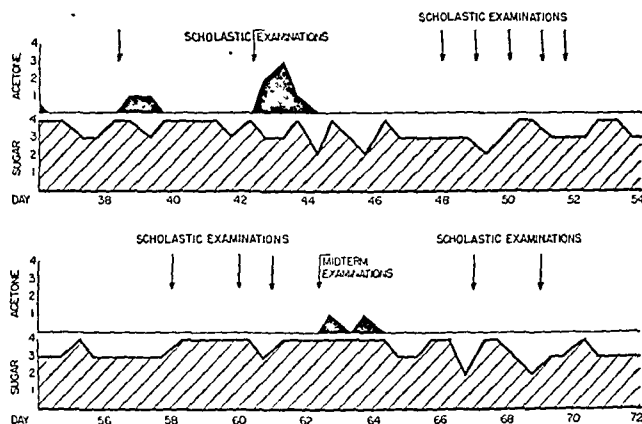


Fig. 13. Further observations on subject of Figure 12 showing the gradual disappearance of episodes of ketonuria when scholastic examinations became less stressful to her.

Ideally, one tries to maintain both the metabolism and behavior of the diabetic person as close to that of the healthy person as possible. It is obvious that treatment limited to the manipulation of diet and insulin cannot attain this goal in many patients, because of their rapidly changing metabolic responses to the events in their daily lives. Furthermore, the craving of many of these persons for food creates an obstacle to precise regulation of their diets. Very few of the persons whom we investigated had even attempted to follow a diet for more than two years, and some of those who tried and thought they were succeeding were found to be making many errors when their daily food intakes were calculated.^{3b}

Knowledge that various forms of life stress may have an important effect on the course of diabetes does not necessarily simplify the treatment of the disease, but in some cases it provides one with another tool for dealing with recurrent episodes of ketosis or hypoglycemia. By studying the patient as a person and obtaining a reasonable understanding of his life history and present life situation, the physician can discover without great difficulty those aspects of his private life which are stressful to him. Sometimes, by discussion with the patient, he can so change his attitude toward persons or situations that events which formerly seemed threatening to him cease to seem so. Sometimes the physician can help the patient to modify his life situation by his own actions or by changes in his behavior. Sometimes he can persuade other persons in the patient's environment to alter their attitudes and behavior for the patient's benefit.

An example of the use of this type of therapy is shown in Figures 12 and 13. The patient, a schoolgirl, 15, was referred to the diabetic clinic because of recurrent episodes of ketonuria, which had continued despite all efforts to abolish them by changes in diet or insulin intake. She was the youngest child of an able family, proud of its intellectual attainments. Her father and brother were physicians; her mother

and civic leader. All three of them expected her to excel in her studies and be a leader in school. They were not sympathetic to adolescent frivolities. The girl, on the other hand, had a mediocre intellect, and longed to take part in the social activities of her friends and schoolmates. In order to meet the demands of her family, she studied for hours each night. She faced the routine daily quizzes of her teachers with great anxiety, mingled with intense resentment because of the burden they placed on her.

The girl had for some time been on a diet carefully prepared by her mother, and each morning 70 units of insulin (25 units of protamine insulin mixed with 45 units of regular insulin) was administered to her by her father. When she was observed carefully, it was found that ketonuria, sometimes associated with thirst and polyuria, occurred whenever she had to face a quiz in

always maintain an interest in what is happening in his patient's life, and give him an opportunity to discuss his problems and seek advice. He should be encouraged to call on the telephone at any time that unusual symptoms develop, for in this manner many episodes of ketosis may be aborted in their incipency. The punitive, restrictive, and rejecting attitudes which the patient so often resents in one of his parents should be carefully avoided. Excessive food intake may be regarded as an expected symptom of the disease. It is our practice to present it to patients as undesirable because it leads to obesity and increased glycosuria, but never as a dangerous or stupid breach of faith. We encourage them to discuss the causes and circumstances of their overeating without fear of rejection or disapproval. Likewise, we encourage a free discussion of conflicts with parents or other members of the family, and accompany it with patient attempts to educate the diabetic in the part which his own attitudes and behavior play in causing them. Discussion with parents, husbands, and wives is often helpful, and sometimes judicious advice for changes in employment or living arrangements may be given. However, great caution should be exercised in advising the separation of adolescents from parents with whom they seem to be in constant and bitter conflict. Often this conflict conceals an intense dependency, and hasty intervention may make the patient sicker rather than better. Patience, forbearance, and a willingness to accept any limited improvement that can be attained is sometimes rewarded with gratifying results.

Effect of Changing Attitudes, Behavior, and Life Situations of Six Representative Labile Diabetics

Patient	Before Treatment	Under Treatment
Typist, 19, female....	12 admissions in coma or severe ketosis in 4 yr.	No admissions in ketosis in 4 yr.
File clerk, 21, female.	2 admissions in coma, recurrent ketosis and polyuria, insulin requirement 90 to 130 units daily for 10 yr.	Asymptomatic, largely aglycosuric, 60 units insulin daily for 2½ yr.
Student, 21, male....	15 admissions in coma or severe ketosis in 6 yr.	Two 21-hr. admissions in mild ketosis in 2½ yr.
Salesman, 29.....	Daily insulin reactions alternating with ketonuria; recently active tuberculosis; unemployed, depressed, anxious; insulin requirement 180 units daily	No insulin reactions, no ketonuria; tuberculosis arrested; steadily employed, mood much improved for 2 yr.; insulin requirement 160 units daily
Schoolgirl, 15.....	Recurrent ketonuria despite careful control of diet and insulin	Ketonuria largely abolished without change in diet or insulin intake
Postmaster, 59.....	Frequent, severe insulin reactions alternating with polyuria and ketonuria; insulin requirement 50 units daily for 10 yr.	Rare, mild insulin reactions, occasional slight polyuria for 2 yr.; insulin intake unchanged

school. The physician did not change her insulin intake or diet. During discussions with her parents he pointed out to them that she had neither the ambition nor the ability to be an intellectual leader but that she had the grace and charm to make a successful marriage. They were persuaded to encourage her in social activities and place less emphasis on studies. Meanwhile, the physician encouraged the girl to feel that the friendships and recreation which she wanted were reasonable and healthy desires for a girl her age. As the attitudes of the various members of the family changed, scholastic examinations became less important to her, and the episodes of ketonuria largely disappeared.

The results which were attained by utilizing such methods in the treatment of six representative patients with labile diabetes from our group are shown in the table. A few of the general principles which were evolved from our experience with the whole group may be outlined briefly. It was found that patients should be seen frequently—at least once a month if they are adolescents or labile adults. After a suitable understanding and rapport is attained between physician and patient, these visits may be brief, but the physician should

SUMMARY AND CONCLUSIONS

Experimental evidence indicates that stressful life situations may lead to important metabolic changes in persons with diabetes mellitus and that these may be accompanied by emotional changes and changes in behavior. Ketonemia and an increased excretion of water, glucose, and chlorides were observed as well as alterations in fasting blood sugar, which might lead to either hyperglycemia or hypoglycemia.

Study of the life histories and daily experiences of persons with diabetes indicates that many of the apparently spontaneous fluctuations in the syndrome are the results of life stress. The similarities in the life histories of these diabetic persons suggests that developmental, cultural, and psychological factors may have an important influence on the onset and course of the disease. Their behavior under stress, their attitudes toward food, and their feelings toward their parents are often so similar as to suggest that these psychological manifestations might be considered as symptoms of the total disease process.

Treatment directed at alteration of the behavior and attitudes of the patient and his relation to his environment is helpful in abolishing otherwise uncontrollable fluctuations in the course of labile diabetes and in preventing recurrent episodes of ketosis requiring hospitalization. In all cases of diabetes an understanding of the patient and his life situation is necessary in order to understand the course of the disease, the limitations of therapy, and the goal which may be attained.

STREPTOMYCIN IN GENITAL TUBERCULOSIS OF FEMALE

FURTHER OBSERVATIONS

Harry Sered, M.D., Frederick H. Falls, M.D.

and

Bruce P. Zummo, M.D., Chicago

Streptomycin has now been used for the treatment of tuberculosis for a period of about six years. A review of the literature fails to reveal any series of significant numbers of gynecologic tuberculosis treated with streptomycin. A preliminary report on 16 cases revealed that results with this antibiotic were encouraging enough to warrant further study.¹

This present communication deals with a follow-up report on our original report, with further studies on 24 additional cases. In those patients who were seen early and who were treated during the relatively incipient phases of the disease, the outcome thus far has been good. As might be expected, in those patients in whom treatment was delayed until lesions were far advanced, less favorable results were obtained. We have observed that, even in far-advanced cases, streptomycin does impede the progress of the disease, and occasionally surprising remissions have been noted. Streptomycin is to be regarded as a most useful adjuvant to present methods of tuberculotherapy in gynecology.

In this series, the patients have been divided into four groups:

A. Those patients in whom genital tuberculosis was diagnosed preoperatively, prepared with streptomycin, operated on, and followed with another course of streptomycin. There are 27 patients in this group, who were unselected and who were referred to us consecutively from other services.

B. Those treated with streptomycin as the sole form of specific therapy in conjunction with the usual conservative measures. There are six patients in this group.

C. Those with gynecologic tuberculosis undiagnosed preoperatively and without the benefit of streptomycin either preoperatively or postoperatively. There are two patients in this group.

D. Those with gynecologic tuberculosis undiagnosed preoperatively but given a full eight-week course of streptomycin postoperatively. There are five patients in this group.

This presentation is primarily concerned with our experience in studying the 27 patients constituting group A, who were operated on and received streptomycin preoperatively and postoperatively.

MEDICAL MANAGEMENT

Dosage.—As a result of our experience with the first 16 cases, it was obvious that equally good results could be obtained when smaller doses were used preoperatively and the time of treatment extended. Accordingly we have standardized the dosage at 1 gm. daily given in a single dose intramuscularly. Oral administration is known to be without beneficial effect in these cases, and subcutaneous injections are much too painful.

As in the treatment of tuberculosis elsewhere in the body, the objective is to produce optimum effects without causing drug-fastness or permanent vestibular damage. There is no single dosage schedule that will give maximum results in the various clinicopathological types of gynecologic tuberculosis. Any plan for treatment should be worked out before actual drug therapy is started. In addition to drug dosage, it is important to focus attention on several other factors: 1. The patient's general condition, including temperature, weight, anorexia, and duration of the disease. 2. Extent of the tuberculous involvement, which includes the essential genital pathology and associated lesions in the lungs, kidney, or other parts of the body. 3. Renal function should be particularly emphasized, since 80% of the streptomycin should be excreted by the normal kidney in 24 hours.² Impairment of this function will predispose to severe toxic reactions. 4. The sensitivity of the organism to the drug as indicated by the clinical response to the drug.

Duration.—Duration of the therapy has been given careful consideration. The objective is to obtain a satisfactory therapeutic effect as rapidly as possible without incurring serious toxic reactions or resistance to streptomycin. In light of the experience gained so far, it was decided that a minimal course of eight weeks of therapy be given preoperatively and at least three weeks postoperatively. This is in accordance with the principle of employing surgery before the appearance of streptomycin-resistant organisms.

The complications encountered to date have been as follows: (1) two episodes of vestibular irritation, one of which responded to a reduction in dose and the other to cessation of therapy, with no further complications on resumption of treatment; (2) heaviness of the head; (3) light headedness; and (4) itching. Two patients became toxic during their postoperative course of treatment.

Clinical Impressions.—Nearly all patients with gynecologic tuberculosis will experience an enhanced sense of well-being early in the course of treatment. The degree and duration of improvement, however, is determined by the amenability of the disease to the antibiotic. Generally, fevers will subside, often within a few days; appetite

The streptomycin for this study was supplied by Merck & Co., Rahway, N. J.

All microscopic sections were read by Dr. Alex Ragins, of the surgical pathology department.

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1. Sered, H.; Falls, F. H., and Zummo, B. P.: Streptomycin in Gynecologic Tuberculosis: A Preliminary Report, *J. A. M. A.* 142: 547-550 (Feb. 25) 1950.

2. The Chemotherapy of Tuberculosis, Rahway, N. J., Merck & Company, Inc., 1950, pp. 7-14.

improve, frequently to the point where the patients cannot get enough to eat; abdominal distention and distress subside, though doughiness will persist; fatigue and weakness diminish as the patient progressively becomes stronger; leukorrhea diminishes; menstrual functions may return in amenorrheic patients; menstrual dysfunction, such as metromenorrhagia, tends to improve; night sweats will most frequently subside; and the occasional patient with diarrhea will show improvement.

Early in our experience we had hoped that the use of the antibiotic, with or without the use of gynecologic surgery, would be of great benefit to those patients who present such combined lesions as gynecologic and pulmonary tuberculosis. It was felt that, after drug therapy, extirpation of diseased genital tissue might enhance the recuperative ability of the extrapelvic organ. Unfortunately, even with the use of streptomycin, our findings do not afford any optimistic prognostications. Those patients who presented serofibrinous or exudative pulmonary lesions seemed to benefit most. The favorable response, however, was probably due to the susceptibility of this type of lesion to the drug, with perhaps some additional therapeutic influence exerted by the pneumoperitoneum as a result of surgery. Those with fibrous or fibrocaceous lesions of the lungs were not demonstrably benefited by the surgical treatment of pelvic pathology. Rather, any brief clinical improvement made by these patients is attributed to the use of streptomycin, as illustrated in the cases reported herein.

REPORT OF CASES

CASE 1.—M. M., whose condition was deteriorating, initially entered the hospital with an exudative process involving the upper lobe of the right lung. Six months later, with the usual conservative treatment, the entire right lung and the lower half of the left lung were infiltrated by tuberculosis; menstrual irregularities were present; and there had been further loss of weight. Endometrial biopsy was positive for tuberculosis. After 65 days of streptomycin therapy, total hysterectomy and bilateral salpingo-oophorectomy were performed. Although her response to streptomycin was slow, she did menstruate on two consecutive months before surgical intervention, and she felt much better despite her failure to gain weight. Three weeks after operation she still failed to gain weight, but roentgenograms of her chest revealed definite signs of healing, and the patient continued to improve during six additional weeks of streptomycin therapy. At present (about two years after surgery) the patient is carrying on her household duties and reports to the board of health clinics for periodic check-up.

CASE 2.—E. M. was septic. After spending six months in the tuberculosis hospital with the usual conservative treatment, she lost 20 lb. (9.1 kg.), coughed more, ceased to menstruate, and suffered intermittent episodes of diarrhea. Endometrial biopsy was positive for tuberculosis. The pulmonary roentgenogram report was "far advanced bilateral acid-fast infection with areas of cavitation in the upper chest bilaterally." One week after the onset of streptomycin therapy, the patient became afebrile, with occasional elevations of temperature to 99.2 F; two full menstrual periods occurred; night sweats subsided; and diarrhea ceased. Up to this time she gained 8½ lb. (3.8 kg.). After 85 days of streptomycin therapy (preoperative and postoperative therapy were extended because of the far-advanced pulmonary lesions) she was subjected to total hysterectomy and bilateral salpingo-oophorectomy. Surgical convalescence was uneventful, and the patient received six weeks of postoperative streptomycin therapy. She then became allergic to the drug, and it was

stopped. When therapy ceased, the patient weighed 98 lb. (44.5 kg.), for a total gain of 19 lb. (8.6 kg.). Two weeks later she began to expectorate blood-tinged sputum, which in staining showed tubercule bacilli. The febrile course recurred, weakness and fatigue returned, and appetite began to diminish, although no masses were palpable. The patient complained of abdominal discomfort, especially after eating. Gradual but progressive weight loss occurred, and the chest x-ray revealed far-advanced cavities of various sizes, with marked fibrotic infiltrations. Smaller doses of streptomycin had no effect. Her prognosis is poor.

Comment.—In none of our patients have we had to cease therapy in less than 120 days. In cases in which favorable results have been obtained initially, the possibility of relapse should be constantly watched for. The two greatest obstacles that have been encountered thus far have been refractory infections, usually in far advanced cases, and extrapelvic recurrences. Unfortunately these relapses do not always respond well, if at all, to further antibiotic therapy.

SURGICAL MANAGEMENT

Surgical Observations.—Although streptomycin will reduce the amount of ascitic fluid in a tuberculous abdomen by inhibiting the peritoneum from secreting more, nevertheless, two patients had up to 1,000 cc. of fluid in the pelvis and abdomen, while six had 300 cc. or less. In most instances of diffuse hyperplastic, adhesive tuberculous infections, it was possible to separate the dense adhesions with surprisingly little difficulty. We were particularly impressed by the seven patients who had been previously operated on and in whom the incision was closed without any attempt to remove the pelvic lesion, because of dense adhesions. Streptomycin seems to reduce the thickness and density of adhesions, facilitating exposure and removal of the diseased organ.

Characteristic of tuberculosis, however, there have been at least three cases in which, despite favorable preoperative subjective and objective findings, abdominal or pelvic findings were not as favorable as expected. In these patients the adhesions remained dense and difficult to separate (lines of cleavage impossible to locate), and surgery was almost as difficult as in those patients operated on without the benefit of streptomycin. In one patient it was so difficult to enter the peritoneal cavity that, even after eight weeks of streptomycin therapy preoperatively, the abdomen had to be closed again without surgical excision. She received six weeks of therapy postoperatively; she was afebrile, comfortable and apparently doing well.

The question poses itself as to whether or not some of these patients with genitoperitoneal lesions ought not have a longer period of preoperative preparation. In the majority of instances an eight-week course seemed adequate, especially since none of them showed any signs of toxicity during this interval. As mentioned previously, two patients did manifest toxic symptoms postoperatively. The answer may lie in the combined use of dihydrostreptomycin and paraaminosalicylic acid. Early results would seem to indicate that such combined therapy tends to inhibit or significantly delay the development of bacterial resistance to the antibiotic.³ This would make possible a prolongation of the effective administration of dihydrostreptomycin and make available a second drug, paraaminosalicylic acid, with demonstrable tuber-

3. The Chemotherapy of Tuberculosis, Rahway, N. J., Merck & Company, Inc., 1950, pp. 18-24. Current Status of the Chemotherapy of Tuberculosis in Man: A Summary Report, Report of the Council on Pharmacy and Chemistry, J. A. M. A. 142: 650-653 (March 4) 1950.

culostatic properties. It remains for the future to determine what effect this combined therapy has on gynecologic tuberculosis with or without surgery.

Surgical Procedures.—In attacking the problem surgically, we were concerned with removal of as much of the pathologically involved tissue as feasible in consideration of the technical difficulties and possible damage to other structures in the pelvis and abdomen. The situation was further complicated by the fact that some of the patients had previously been operated on at intervals varying from a few weeks to several years, either for tuberculosis or for some other form of pelvic disease.

In this series we have continued to practice early ambulation, allowing the afebrile patients out of bed on the second or third day. This was followed by no untoward after-effects.

The surgical management of these patients must of necessity take into consideration the many complications that the patients present which are unrelated directly to the pelvic disease. These complications have been divided into three categories: (a) those occurring before surgery, including active pulmonary tuberculosis in 3 instances, pleurisy with effusion 4, tuberculosis of the cervix 4, breast abscess 1, tuberculosis of the brain 1, thoracoplasty 1, and intestinal obstruction 1; (b) those occurring during surgery; and (c) those arising after surgery.

Nine patients had been subjected to previous pelvic surgery elsewhere. Three had subtotal hysterectomies; one was operated on for small bowel obstruction (and postoperative adhesions); in one the incision was made for pneumoperitoneum effects; and in four cases of exploratory surgery prompt closure followed the discovery of inoperable tuberculosis. The preoperative diagnosis in these four patients were (a) left tubo-ovarian abscess, (b) interval appendicitis and chronic salpingitis, (c) tuberculous adnexitis, and (d) chronic salpingo-oophoritis. After transfer to our service, they were then given a course of streptomycin and reoperated on with good results.

Of the 27 patients who have been operated on by us, the following procedures were done: total hysterectomy and bilateral salpingo-oophorectomy, 16; total hysterectomy and unilateral salpingo-oophorectomy, 2; total hysterectomy, bilateral salpingectomy, and unilateral oophorectomy, 3; and subtotal hysterectomy and bilateral salpingo-oophorectomy, 3.

Pathologic Findings.—In order of frequency, the tuberculous pathologic findings were as follows: peritonitis in 27 cases, salpingitis (with or without oophoritis) 24, endometritis 16, diffuse adhesions 11, ascites 8, oophoritis 4, tubo-ovarian abscesses 4, lymphadenitis 3, ovarian caseation necrosis 3, and myometritis 1. Interesting additional nontuberculous findings were as follows: 1 dermoid tumor and 1 pseudomucinous cyst. In 16 instances in which particular study of the oviducts was made, 6 were noted to be patent and 10 were occluded. Of the 7 cases of tuberculous oophoritis, 3 were of perioophoritis and 4 of the interstitial type. Three patients had ovarian caseation necrosis, and all were grossly found by bisection of the ovary during surgery.

Continuing the attempt to determine the effect of streptomycin on the tuberculous process, tissue and fluid have been removed during surgery for culture, smear, and guinea pig inoculation. Of the 14 results thus far returned, six were positive for tuberculosis and eight were negative. One of the negative reports was noted in a patient who subsequently died, nine months postoperatively. In another patient with negative reports, tuberculous nephritis developed 18 months postoperatively.

Complications.—During surgery, cystotomy occurred accidentally in one patient. Postoperatively, fecal fistula developed in 2 patients, wound infections in 3, and carcinoma of the cervix in 1. The first fistula developed two months after surgery in a patient who became resistant to streptomycin and subsequently died. The second fistula developed in a patient with far-advanced tuberculosis of the pelvis and abdomen and who had a previous spontaneous tuberculous fistula that responded to streptomycin-phthalylsulfathiazole treatment. She was subjected to surgery after a 120-day course of streptomycin and a two-month delay for convalescence. Her postoperative fistula appeared at the identical site one week after surgery but responded to streptomycin and sulfathaladine. At present she is doing well, and no further complications have been noted. The patient with carcinoma of the stump will be discussed later.

FOLLOW-UP STUDIES

Every four weeks these patients return for follow-up studies. They are requested to make daily temperature and weight recordings and to keep track of any noteworthy incidents, such as vasomotor changes, gastrointestinal symptoms, chills, fevers, and night sweats. Pelvic examinations are done on all patients. Roentgen studies of the chest or bowel are made whenever deemed necessary. In those patients who had subtotal hysterectomies, the cervical stumps are closely observed for any abnormal changes.

There have been two deaths in this series, both occurring in patients with advanced lesions.

CASE 3.—M. S. died three months after surgery. (This case has been reported in detail in our previous publication.¹) Briefly, she was a 40-year-old Negro woman, in very poor condition when first seen. The patient made surprising improvement during intensive streptomycin therapy for 50 days. A total hysterectomy and bilateral salpingo-oophorectomy were done. Her postoperative course was uneventful, and the patient was discharged 14 days later. She continued to do well until six weeks after surgery, when a partial bowel obstruction developed. Although responding to conservative measures of Levine suction, oil and enema regimen, and streptomycin therapy, her symptoms recurred, resistance to the drug developed, and the patient became worse. A spontaneous ileostomy developed, and the patient died shortly thereafter.

CASE 4.—E. A., a Negro woman, 21, entered the gynecologic service in August, 1948. She was described as being acutely ill, thin, with a temperature of 101 F, a pulse rate of 124, and respiratory rate of 24. Her complaints were 30 lb. (12 kg.) weight loss, abdominal distention and discomfort, a good appetite but unable to eat because of associated abdominal discomfort with ingestion of food, and markedly increased whitish vaginal discharge. She had missed her last two menstrual periods. Chest x-rays did not reveal any cardiac or pulmonary abnormalities. Barium roentgenograms were interpreted as presenting "changes compatible with clinical impression of tuberculous peritonitis." The corpus uteri was pushed upward by adnexal masses, deviated

to the left, of normal size, and apparently fixed to the underlying masses. The vaginal discharge was purulent and cheesy. Endometrial biopsy revealed "necrosis of the caseating type." Cervical biopsies were negative for tuberculosis. Streptomycin was given for 54 days, whereupon surgery was performed. Grossly there was noted diffuse adhesions and lymph nodes everywhere. Bisection of these nodes revealed caseous contents. Total hysterectomy and bilateral salpingo-oophorectomy were done. Microscopic findings were tuberculous endometritis, myometritis, cervicitis, salpingo-oophoritis, and caseation of a lymph node.

Streptomycin therapy was continued for three weeks postoperatively. The patient was seen every four weeks for the next six months. During this interval she gained 22 lb. (9.1 kg.), was afebrile, and had an enormous appetite, minimal vasomotor symptoms, and no gastrointestinal complaints. On the eighth postoperative visit, she had lost 3 lb. (1.3 kg.), complained of occasional headaches, and felt weaker. Hospitalization was refused. In August, 1949, (nine months after surgery), she was readmitted to Cook County Hospital complaining of severe headaches and diplopia. The neurosurgeon thought an intracranial tumor probable. Exploratory trephining revealed a tuberculoma of the brain. The patient was given six weeks of streptomycin and became asymptomatic. Two weeks later her complaints recurred, followed by stupor, coma, and death. Permission for autopsy was not granted.

Other complications thus far encountered in this follow-up series were tuberculous nephritis (Case 5), carcinoma of the cervix (Case 6), and nontuberculous cystic changes of retained ovarian tissue (Case 7).

CASE 5.—A. W., a 15-year-old Negro girl, was admitted to the surgical service complaining of premenstrual discomfort in the right lower abdominal quadrant, lasting through the first day of flow, and temperature up to 101 F. At the time of admission the abdominal distress had been continuous for four days. After six days of sulfadiazine and penicillin therapy, the patient was subjected to surgical exploration. When the abdomen was opened, adhesive hyperplastic tuberculosis was noted everywhere, so that no further attempt at surgery was made. After eight weeks of streptomycin therapy, supracervical hysterectomy and bilateral salpingo-oophorectomy were done. Bilateral tubo-ovarian masses, containing necrotic caseous material, were found. She was given three weeks of streptomycin therapy postoperatively. The patient did remarkably well for the next 18 months but began to complain of urinary frequency and urgency, nocturia, and questionable hematuria. Urine cultures were positive for tuberculosis. At present she is receiving streptomycin and paraaminosalicylic acid and apparently doing well.

CASE 6.—A. R., a 49-year-old Negro woman, was admitted to Cook County Hospital, April 22, 1949, complaining of abdominal swelling, weight loss, fever, and chills. Roentgenograms of the chest and gastrointestinal tract were not noteworthy. In 1920 she had been subjected to supracervical hysterectomy and unilateral salpingo-oophorectomy. Preoperative clinical biopsies revealed chronic cervicitis. After eight weeks of streptomycin therapy she was operated on. Dense diffuse adhesions were found everywhere; because of technical difficulties, only salpingo-oophorectomy was possible. Her postoperative course was uneventful, and she received streptomycin for three weeks during convalescence. During routine follow-up examinations she was subjected to a fifth cervical biopsy, and on this occasion a "definite non-hornifying squamous cell carcinoma" was found. The patient has thus far received a one-week course of radium therapy (seven needle implants of 2 mg. each) and a full course of roentgen therapy. Postradiation biopsies have been negative for carcinoma.

CASE 7.—E. B., a 29-year-old Negro woman, entered Cook County Hospital May 15, 1948, complaining of prolonged menses, left lower abdominal quadrant discomfort, weight loss, fever, and chills. She was treated for a pelvic inflammatory process with sulfadiazine and penicillin, but the response was not satisfactory. Endometrial and cervical biopsies were positive for tuberculosis. Streptomycin almost immediately made her afebrile. After six weeks of drug therapy she had a total hysterectomy and bilateral salpingectomy. After three weeks of

postoperative streptomycin therapy, she left the hospital in good condition. She felt well until Jan. 9, 1950, when a cystic mass the size of an orange was palpated in the region of the rectum sigmoid. Barium roentgenograms and sigmoidoscopy failed to reveal any large bowel pathology. On January 31 a laparotomy was done. Minimal adhesions were found, and a multilocular cyst was resected. The pathology report stated there were several pieces of tissue containing several hemorrhagic cysts, the smallest fragment being composed of corpus luteum. Microscopically it was found to contain "much blood and fibrous connective tissue, and suggestive dependent granulosa cells." At present the patient is doing well.

Cases in Groups B, C, and D will not be discussed in detail. Of the six patients in Group B, treated with streptomycin as the sole form of therapy, one patient died and five are alive and doing well. All, however, show manifest residual adnexities and doughy abdomen. The one death occurred in a Negro woman (G. L.) with advanced pelvoabdominal tuberculosis as well as "lateral pneumonitis, acid fast, with cavitation in the left apex." She died four months after admission, deriving little if any benefit from drug therapy. The two patients in group C who were operated on without streptomycin therapy at any time, began to show signs of complications 7 months and 13 months, respectively, postoperatively. F. A., a Negro woman of 36, had a total hysterectomy, bilateral salpingectomy, and left oophorectomy. Seven months later we were able to palpate a doughy mass, the size of an orange, replacing the right adnexa (ovary). She refused further surgery. P. A., a Negro woman of 24, had a subtotal hysterectomy and a bilateral salpingectomy. Thirteen months later a cystic mass, the size of a grapefruit, was palpated in the region of the left iliac fossa. She also refused further surgery. In both instances, barium roentgenography was negative for bowel pathology.

Of the five patients in Group D, who received streptomycin therapy postoperatively only, two had fecal fistulas, arising as a result of bowel injuries. In both patients the rent in the large bowel was sutured without benefit of colostomy or ileostomy. The fistulas developed 5 days and 18 days, respectively, after surgery. The first closed spontaneously with streptomycin and phthalylsulfathiazole therapy. The second patient, although receiving identical drugs, had a transverse colostomy done at the time of the operation and is under the care of the surgical department.

SUMMARY AND CONCLUSIONS

1. Two and one-half years' clinical experience with the use of streptomycin in 40 patients with gynecologic tuberculosis is herewith reported. These patients have been divided into four groups, each with different mode of treatment. The immediate and follow-up findings are reported.

2. Experience seems to favor a dosage of 1 gm. streptomycin injected intramuscularly daily.

3. A period of eight weeks or more of preoperative streptomycin preparation improves operability and final results.

4. One of the most frequent but not commonly discussed complaints is the presence of a good appetite and unwillingness to eat because of postprandial pain.

5. Decrease in postprandial pain after treatment with streptomycin permits the ingestion and better digestion of food.

of more food, which helps to improve the general condition and makes the patient a better operative risk.

6. Nearly all patients with gynecologic tuberculosis will experience an enhanced sense of well-being early in the course of treatment. The degree and duration of improvement is determined by the amenability of the disease to the antibiotic.

7. The most persistently good responses are noted in patients in whom therapy is instituted relatively early.

8. As in other forms of tuberculosis, recurrences elsewhere must be anticipated. Negative smears, cultures, and guinea pig inoculations of excised surgical tissue do not preclude this possibility.

9. Radical extirpation of diseased tissue, when feasible, is the treatment of choice. Total hysterectomy and bilateral salpingo-oophorectomy were done whenever possible. The follow-up studies on all four groups would seem to justify this procedure.

10. Removal of pelvic tuberculous lesions, supplemented by streptomycin therapy has no beneficial influence on associated advanced pulmonary lesions.

11. In order of frequency, the tuberculous pathologic findings were peritonitis, salpingitis, endometritis, diffuse hyperplastic adhesions, ascites, oophoritis, cervicitis, tubo-ovarian abscesses, lymphadenitis, ovarian caseation necrosis, and myometritis. Six oviducts were patent, and 10 were closed.

12. There have been two deaths in 27 surgical cases, both occurring in patients with far-advanced lesions. The complications encountered during this period have been (a) streptomycin resistance with miliary spreads, (b) tuberculoma of the brain, (c) tuberculous nephritis, (d) carcinoma of the cervix, and (e) nontuberculous cystic changes in retained ovarian tissue.

13. The persistence of doughy abdomen has been a common finding during the follow-up interval of two and one-half years.

14. Streptomycin is to be regarded as a most useful adjuvant to present accepted methods of therapy in gynecologic tuberculosis.

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PHYSICAL MEDICINE PLUS CORTISONE FOR RHEUMATOID ARTHRITIS

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and

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Because of the recent interest in cortisone and corticotropin (ACTH) in the treatment of rheumatoid arthritis, physical medicine and other measures that are of proved value in the management of patients with rheumatoid arthritis have been slighted. The purpose of the present study is to evaluate the relation of physical medicine to cortisone in the treatment of such patients.

As the treatment with cortisone of increasing numbers of patients having rheumatoid arthritis has continued, it has become apparent that cortisone alone, as it is customarily used at present, does not always provide complete control of the disease. It is well recognized, as has been reported,¹ that cortisone alone will relieve much of the pain and stiffness and will produce a decrease in the synovial inflammatory reaction. However, in order for many patients with rheumatoid arthritis to obtain maximal objective signs of improvement in articular function while receiving safe suppressive doses of cortisone, it is essential to utilize a program of treatment that includes physical medicine.

This study is based on a comparison of the results of treatment of two groups of patients hospitalized with rheumatoid arthritis. One group received a conservative program that included physical medicine measures, adequate rest, salicylates, proper diet, and, in some instances, special articular supports when indicated. The other group of patients received similar conservative treatment plus cortisone.

The physical medicine program, described elsewhere in detail,² consisted essentially of daily systemic heating for 30 minutes accomplished by the application of luminous infra-red bakers, by means of a hot tub bath with

a water temperature of 102 to 104 F or by a hot moist-air "fever cabinet," the latter two methods raising the patient's oral temperature to 100 to 101 F. The application of heat was followed by light to deep stroking and kneading massage of the affected extremities. The exercise program consisted of active and assistive exercise to attempt to increase the range of motion. When indicated, resistive exercises were prescribed to increase strength of muscles. Gait training made up an essential part of the exercise program of many of the patients, some of whom were taught to eliminate a limp, others how to get in and out of chairs, how to use crutches or canes properly, and how to determine the amount of walking or other activity that could be tolerated.

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From the Section on Physical Medicine and Rehabilitation, Mayo Clinic (Dr. Martin); Division of Medicine, Mayo Clinic (Dr. Polley); Fellow in Physical Medicine, Mayo Foundation (Dr. Anderson).

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2. Polley, H. F.: Physical Medicine in the Care of Rheumatoid Arthritis, South. M. J. 10: 596-600 (July) 1947. Kendall, H. W.; Polley, H. F., and Krusen, F. H.: Physical Medicine in the Home Treatment of Arthritis, Rheumatism 3: 86-88; 103-104 (April-June) 1947. Erickson, D. J.: Physical Medicine for the Homebound Arthritic, Brit. J. Phys. Med. 13: 193-197 (Sept.) 1950.

Since the effects of cortisone alone for patients with rheumatoid arthritis are well known and have been reported, no group of patients treated solely with cortisone is included in this study. The dosage and schedule for the administration of cortisone were determined by the apparent requirements of the individual patients. After treatment was begun, repeated efforts were made

TABLE 1.—Results of Treatment of Patients with Rheumatoid Arthritis Based on Objective Changes in Articular Function

Objective Changes in Articular Function	Physical Medicine		Physical Medicine and Cortisone	
	Patients	%	Patients	%
Marked improvement.....	5	14.7	10	18.5
Moderate improvement.....	22	61.7	36	66.7
No change.....	7	20.0	8	14.8
Total.....	34		54	

to lower the dosage and to determine the minimal maintenance dose. These maintenance doses were usually less than 100 mg. per day.^{2a} However, they have the advantage of producing fewer undesirable physiologic and psychologic side-effects. With these smaller doses, the signs and symptoms of the rheumatoid arthritis may be suppressed but are not necessarily completely controlled.

SELECTION OF PATIENTS

Eighty-eight patients with rheumatoid arthritis were included in this study; 55 were female and 33 were male. Their ages ranged from 4 to 73 years. The duration of the symptoms varied from less than one year to more than 20 years. A definite diagnosis of rheumatoid arthritis could be made in all patients. The activity of the arthritis in all patients was moderate to severe, and all the patients were hospitalized for periods ranging from two and a half weeks to more than a year. Patients included in the study had repeated measurements of range of motion in joints with limitation. The larger joints, such as the knees, elbows, and shoulders, which permit fairly accurate goniometric readings, were used whenever possible. Arthritic patients receiving treatment other than as defined in previous paragraphs or having other associated diseases were excluded from the study. Evaluation of the treatment programs was based on results occurring during the period of hospitalization.

The subjects were divided into two groups of about equal age and sex distribution and with comparable degrees of rheumatoid arthritis. Group 1 consisted of 34 patients treated with a conservative program in which physical medicine provided an essential part of the therapeutic regimen. These patients in Group 1 were all chosen from those treated since 1948, in order that the physical medicine and other conservative measures would be comparable to those received by the subjects in Group 2. Group 2 consisted of 54 patients who received cortisone in addition to physical medicine and other supportive treatment. These patients in Group 2 were hospitalized during 1950 and up to April, 1951.

The effects of the treatments on articular function were evaluated as objectively as possible. Measurements of the range of motion of the joints were made at intervals of at least one week. Significant changes in the patient's means of locomotion with a description of the type of ambulation attained were utilized as other signs of objective improvement. Although the majority of patients (particularly in the group receiving cortisone) showed varying degrees of subjective improvement these factors were not included as criteria for improvement in this study.

RESULTS

In classifying the results of treatment, we used three general groups: (1) those showing marked improvement in the articular function and ambulation, (2) those showing moderate degrees of improvement, and (3) those showing no significant improvement during the period of hospitalization. The first group consists of patients who made outstanding or marked improvement in articular function and in ambulation during the period of observation. For example, an improvement from 150 degrees to 175 degrees in extension of the knee occurring in a period of less than three months was considered as evidence of marked objective improvement. In most instances, this increase in range was associated with marked improvement in ambulation. A patient who entered the hospital bedridden and was able to leave walking with crutches or canes was included in this group. The second group includes the patients who showed moderate degrees of improvement in range of motion as well as some significant improvement in the locomotion. An improvement of 10 degrees in extension of the knee, for instance, with a change from 160 degrees to 170 degrees would indicate a moderate degree of objective improvement in articular function. The third group includes those who showed no significant improvement in articular function. This applied particularly to such weight-bearing joints as the knees and hips. For instance, a patient with no significant increase in range of motion of flexed knees, even though he showed slight improvement in the shoulders, would be included in this group.

TABLE 2.—Results of Treatment of Patients with Rheumatoid Arthritis in Relation to Duration of Symptoms

Duration of Symptoms, Yr.	Physical Medicine			Physical Medicine and Cortisone		
	Patients	No. Improved	%	Patients	No. Improved	%
0-1.....	8	8	100.0	7	6	85.7
1-4.....	10	9	90.0	13	11	84.6
5-9.....	9	6	66.7	13	11	84.6
10+.....	7	4	57.1	21	18	85.7
Total.....	34	27	79.4	54	46	85.2

The results of the two programs of treatment are summarized in Table 1. The percentage of patients showing marked to moderate improvement in the two groups was about the same, except that of the subjects who received physical medicine without cortisone a slightly larger percentage showed no significant change than was observed in the group receiving physical medicine plus cortisone.

From analysis of the results of the two treatment programs in relation to the duration of the patient's illness (Table 2), it appears that as the duration of the sym-

2a. Ward, L. E.; Slocumb, C. H.; Polley, H. F.; Lowman, E. W., and Hench, P. S.: Clinical Effects of Cortisone Administered Orally to Patients with Rheumatoid Arthritis, *Proc. Staff Meet., Mayo Clin.* 26: 361-370 (Sept. 26) 1951.

toms increases, the percentage of patients showing improvement with conservative treatment decreases. When the rheumatoid arthritis had been present for five years or longer, the percentage of patients showing improvement was greater in those treated with physical medicine plus cortisone (85.7% to 84.6%) than in those treated with physical medicine alone (57.1% to 66.7%).

TABLE 3.—Results of Treatment of Patients with Rheumatoid Arthritis in Relation to Duration of Treatment

Duration of Treatment, Mo.	Physical Medicine			Physical Medicine and Cortisone		
	Pa-tients	No. Im-proved	%	Pa-tients	No. Im-proved	%
Less than 1.....	12	11	91.7	8	8	100.0
1-2.....	16	12	75.0	30	24	80.0
More than 2.....	6	4	66.7	16	11	87.5
Total.....	34	27	79.4	54	43	85.2

The results of the two programs of treatment were further analyzed in relation to the duration of hospitalization, which in general paralleled closely the duration of treatment (Table 3). However, in several of the subjects with prolonged hospitalization (more than two months), the period of administration of cortisone was considerably shorter than the total hospitalization. The best results were obtained in the patients needing treatment for relatively short periods. This may be explained on the basis of the relatively milder disease present in these cases at the time of treatment. Patients with more serious involvement as well as those who were more resistant to treatment were treated for longer periods. The percentage of those showing improvement from the long-term program in these cases was somewhat less. For the patients treated for two months or longer, there is a greater likelihood of obtaining improvement with physical medicine plus cortisone (87.5%) than with physical medicine and other conservative measures without cortisone for the same period (66.7%).

Analysis of data on patients grouped according to age indicated comparable results. Apparently age is not a determining factor in whether or not the younger or older patients are more or less likely to respond to one or the other of the therapeutic programs.

REPORT OF CASES

Physicians treating arthritic patients have long recognized that the treatment of patients with rheumatoid arthritis must be highly individualized. Analysis of the group results of treatment has indicated the value of physical medicine either alone or combined with cortisone. However, the presentation of several individual reports of cases will serve to elucidate some of the therapeutic problems that may be encountered. The cases on which data are to be presented illustrate some of the widely varying manifestations occurring in rheumatoid arthritis.

The first patient was in the younger age group and had a shorter duration of symptoms of rheumatoid arthritis. The patient obtained marked improvement with a relatively short period of treatment with cortisone plus physical medicine. The second patient had chronic rheumatoid arthritis with flexion deformities and showed no significant effective change either with prolonged physical medicine alone or with a program of cortisone

plus physical medicine. The report of the third case illustrates what was accomplished with one patient by a conservative program alone. This patient had previously received cortisone alone (elsewhere), with no significant improvement. Case 4 illustrates some of the things that were accomplished in a severely involved chronic rheumatoid arthritic patient by use of a combined treatment program plus orthopedic measures over a prolonged period.

CASE 1.—A Negro woman, aged 18, had active rheumatoid arthritis of one and a half years' duration. The shoulders, elbows, wrists, and knees were involved. There was a flexion contracture of the right knee with marked synovitis. Narrowing of the joint space was noted on roentgenographic examination. This joint was so painful that the patient had not walked for one month prior to admission. She was hospitalized for 42 days of treatment. She received cortisone, 100 mg. per day for nine days, at the end of which time pain and limitation of motion in the involved joints had improved approximately 50%. Physical medicine was then prescribed, including heat, mild fever therapy, massage, exercise, and gait training. The dosage of cortisone was gradually reduced to 50 mg. per day. Range of motion in the joints improved further, with the right knee and left elbow regaining full motion. The patient was taught to walk in parallel bars and gradually progressed to walking with two canes, then with one cane; finally she was able to walk without a cane, with no limp and without pain in the right knee. The sedimentation rate dropped from 117 mm. in one hour to 51 mm. in one hour (Westergren). The patient gradually gained weight and was generally improved.

CASE 2.—A white woman, aged 57, had severe chronic rheumatoid arthritis of six years' duration. She had marked flexion contractures of the hips and knees. Roentgenograms of these joints showed advanced degenerative changes with narrowing of the joint spaces. The sedimentation rate was 50 mm. in one hour. She was hospitalized for 37 days of treatment. Physical therapy, consisting of heat, massage, and exercise, had been started several months prior to hospitalization and was continued during hospitalization in addition to other supportive measures. A splint to increase extension of the right knee was used. Administration of cortisone was started on the fifth day of hospitalization. Doses were 100 mg. per day for six days and then 50 mg. daily for eight days, then 200 to 275 mg. per week. There was no objective improvement on this program. The patient remained nonambulatory. Subjective improvement was slight, and the pain in the knees continued even at rest. Treatment has been continued for six months since hospitalization, with no essential change in function because of previously damaged joints.

CASE 3.—A white woman, aged 63, had severe chronic rheumatoid arthritis of three years' duration. She had marked flexion contractures of the knees and 50% limitation of left shoulder abduction. There was generalized osteoporosis with compression fractures of six vertebrae. The sedimentation rate was 105 mm. in one hour. The patient had been given cortisone irregularly for five months prior to admission. She was hospitalized for 100 days and treated without further use of cortisone. Physical medicine, consisting of heat, massage, exercise, and gait training, was started on the 30th day. The patient wore a Taylor back brace during physical activity. The response to this treatment program was excellent. The knees straightened from extension of 140 degrees to 175 degrees. The left shoulder regained full range of motion. She progressed from being nonambulatory on admission to walking in parallel bars during the sixth week, to walking with crutches during the seventh week, to walking with glider canes for four days during the eighth week, and thereafter to using one cane for walking and climbing stairs. The sedimentation rate dropped from 105 mm. in one hour to 88 mm. in one hour. The patient's general condition improved markedly.

CASE 4.—A white man, aged 29, had severe chronic rheumatoid arthritis of six years' duration. He had been nonambulatory for four years. There were extensive osteoporosis and marked muscular atrophy. The hands were severely deformed with limited motion and hyperextension of the proximal interphalangeal joints. He had marked flexion contractures of both wrists and

knees, with slight subluxation of the latter. Roentgenograms of the knees showed narrowing of the joint spaces with slight destructive changes. He was hospitalized for the 13 months preceding June, 1951. The knees were manipulated with the patient under anesthesia, and a moderate increase in extension was obtained. Physical medicine was started two days after the manipulation. This treatment included heat, hydrotherapy, massage, and exercise, which was cautiously undertaken because of the severe osteoporosis. Gradually, moderate improvement was made with this program. When the knee extension became 160 degrees, walking with assistance was started. After two months on this program, administration of cortisone was started in daily doses varying from 100 mg. to 50 mg. One month later the knees attained full extension. Arthrodeses of the wrists in a functional position helped in making the hands more useful. Progression in ambulation was carried out with great caution because of the severe osteoporosis. By the eighth month the patient could walk unassisted. Attempts to reduce the dosage of cortisone resulted in flare-ups which temporarily restricted physical activity. Increasing the maintenance dose slightly again has permitted more active physical medicine. The patient has been receiving cortisone for 11 months and physical medicine for 13 months. Physical medicine alone did not provide adequate treatment for this patient, and it is doubtful that cortisone alone would have been any more adequate. With combined treatment, certainly the moderate degree of improvement that has occurred in this patient has considerably improved his ability to be self-dependent and ambulatory.

COMMENT

A carefully supervised conservative program including physical medicine, adequate rest, diet, simple analgesics and other general supportive measures is of much value in the treatment of rheumatoid arthritis. Results of such a program, as indicated in a selected group of patients in this study, were favorable even before the advent of cortisone. This study, nevertheless, indicates that cortisone is an important adjunct to the treatment program of many patients with active rheumatoid arthritis. Not only may the symptoms be decreased significantly in the patients in the active phase of rheumatoid arthritis but, also, considerably more can be accomplished in a large percentage of the patients who have severe and more chronic involvement and who require long periods of supervised medical care to control the active rheumatoid arthritis. Cortisone will suppress or relieve the symptoms of stiffness and pain and diminish the inflammatory reaction. As has been pointed out,³ mobilization of joints can be accomplished by cortisone with the addition of physical medicine in patients who otherwise might obtain only limited improvement with physical medicine and other conservative measures alone. As Hench^{1b} has said, "Cortisone suppresses the fire; it does not of itself put out the fire (remove the irritant) nor does it serve as a carpenter to repair the fire's damage." Even with the combined treatment in some of the severely disabled patients, significant results may be achieved only very slowly, if at all.

It is sometimes difficult to predict the degree of improvement that may be achieved in some of the severely involved patients. This is illustrated by Case 3, in which cortisone alone given elsewhere produced little or no significant improvement, at least by the schedule used, but later during hospitalization without cortisone and with a conservative program including physical medicine, satisfactory objective improvement occurred. On

the other hand, in Case 4, the results were better with cortisone and physical medicine than could have been expected with either alone. It can be anticipated that results will generally be rather limited when articular dysfunction is more the result of damage already done to the joint than the result of active inflammation.

Cortisone has been used therapeutically for only a very short period, and much remains to be learned regarding optimal methods of administration. However, in all instances dosage of cortisone must be carefully adjusted to provide optimal relief with minimal risk of undesirable side-effects. Likewise the physical medicine program must be carefully prescribed for each patient.⁴ Exercise tolerances vary widely, and the ability to progress from active assistive exercise to resistive exercise and increase ambulation needs to be carefully determined and regularly supervised.

SUMMARY

Eighty per cent of a group of 34 patients with moderate to severe rheumatoid arthritis treated with physical medicine and other conservative measures showed objective evidence of improvement in articular function and ambulation. Eighty-five per cent of a similar group of 54 patients who were treated with cortisone in addition to physical medicine and other conservative measures showed objectively improved articular function. Patients with rheumatoid arthritis who have limitation of articular function and who are receiving cortisone may benefit further by a carefully prescribed and supervised program of physical medicine. In all instances, the treatment program must be individualized, since the requirements for physical medicine and cortisone vary widely in different cases.

3. Polley, H. F., and Elkins, E. C.: Significance to the Physiatrist. Recent Developments in Rheumatic Diseases, *Arch. Phys. Med.* 32: 1-151 (March) 1951.

4. Martin, G. M.: What Every Physician Should Know About Prescribing Physical Therapy, *J. A. M. A.* 142: 474-476 (Feb. 18) 1950.

Abdominal Percussion.—Percussion of the abdomen is a well recognized aid in outlining an enlarged liver or spleen, in determining the presence of free fluid, in delineating the size of an ovarian cyst, an enlarged uterus, or a distended stomach. Its usefulness in the presence of peritoneal inflammation has been generally overlooked. . . . To me it is the most helpful single diagnostic procedure in evaluating the acutely disturbed abdomen. Long since discarded has been the sign of "rebound tenderness." It is gross, it is cruelly painful, and it is not sufficiently accurate to be helpful when most needed in locating the primary seat of inflammation. In the appraisal of an abdomen under scrutiny, the patient is not touched until he has been asked to cough. The resulting pain will give the first evidence of the site of inflammation, and of the probable organ or viscus primarily involved. The abdomen is then palpated to determine the presence of muscle guarding. This must be done gently, and painlessly, and is begun in areas away from the site of pain revealed by coughing. Rarely is guarding absent over areas of inflammation, but it cannot be accurately located by a hand. . . . Then follows light percussion—also begun in presumably unaffected areas—by working downward from the epigastrium in lower abdominal discomfort, toward the epigastrium in upper abdominal pain, and from the side of comfort to the side of pain in unilateral involvement. The area of tenderness is quickly and easily ascertained. . . . —Emile Holman, *The Art of Abdominal Percussion in the Presence of Inflammation*, *Surgery, Gynecology and Obstetrics*, December, 1951.

ERASMUS AND HIS DISEASES

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Anyone who has had the pleasure of studying at, or of visiting, Cambridge University, England, will remember Queens College. Queens College, the second royal institution in Cambridge, was established by Margaret of Anjou, queen of Henry VI, in 1448. Andrew Dokett was its first president, and held the office for many years. The college, which is famous for its principal court, gate house, and great gateway, was completed in 1451 and still functions. There are several courts and cloisters, varying in their dates of establishment. All of them are beautiful, as well as ancient, and Pump Court is especially renowned as being the study of the scholar, Erasmus. It is appropriately called Erasmus Tower. In the gallery of the President's lodge there is a high, stiff, uncomfortable chair—Erasmus' chair. Just across the river Cams, there is a walk in the college gardens known as Erasmus' Walk. Erasmus was in residence at Queens' from 1510 to 1513 and was the first man to teach Greek at Cambridge.

Desiderius Erasmus,¹ Dutch scholar, hygienist, humanist, theologian, and world traveller, was born out of wedlock in or near Rotterdam in October, 1466. His mother, the daughter of a physician, died of the plague when he was 13 years of age, and his father died shortly thereafter, leaving him and his brother, Peter, under the care of three guardians. Erasmus preferred a university training, but they sent him to an Augustinian monastery at Gouda and later to Deventer, where he studied with a famous scholar, Alexander Hegius. Erasmus is said to have had a wonderful memory and could recite all the works of Horace and Terence. He was ordained a priest at Steyn and later studied at the University of Paris, where he received his B.D. degree. While in Paris, he met an Englishman, Baron Mountjoy, afterward, tutor for Henry VIII, with whom he spent several months at Oxford. Later he returned to Paris for further study in Greek. He had already published a small book of poems, and in 1504, his "Annotations on the New Testament" was printed by his friend Badius. After another visit to England, further studies were carried on in Italy at Turin and Bologna. A new edition of his "Adagia" ("Familiar Quotations from the Classics") was published, with Erasmus' help, by the Venetian printer Aldus Manutius. He returned to England and taught Greek in Cambridge University from 1511 to 1514. He then went to Basel, Switzerland, in connection with the publication of some of his writings by the celebrated printer Johann Froben. This relationship lasted until Froben's death. Erasmus did much of the writing and editing, and Froben did the printing, while the illustrations were done, for a while, by Holbein. This combination made Basel the center of the printing industry in Europe.

In his time it was not safe to live outside a walled town or city. He dwelt in Basel on a street called Bäumlein Gasse (little tree-street). Because of his arthritis, he had an open fireplace, but the wood was expensive. He was invited to the University of Leipzig and to the University of Ingolstadt (later called Munich). Archduke

Ferdinand offered him a pension if he would come to Vienna. He was made counsellor to Charles of Austria, later Charles V of Germany. He preferred Basel, which his friend, Beatus Rhenanus, termed the "queen of cities." After Froben's death, Beat Bild² (Beatus Rhenanus) assisted with the publishing. Bild received an M.A. at Paris. His library has survived almost intact, including a large number of Erasmus' letters, and is now part of the town library at Schlettstadt. Bild came to Basel from Schlettstadt, and associated himself as corrector of press with Erasmus as editor. Froben's son, Hieronymus, and Bonifazius Amerbach were the printers, Gerbell and Oecolampadius, correctors of proof, and Graf and Holbein provided the illustrations. The painter and etcher Albrecht Dürer also resided there for a time and made portraits of Erasmus. Sebastian Brant, who wrote one of the earliest and rarest books on syphilis, was also a citizen of Basel.

ERASMUS AS AUTHOR

As Smith³ remarks: "Erasmus represented better than any other one man the common spirit of the Renaissance." He spoke French, English, and Italian, but used Latin for writing and ordinary conversation. He translated the New Testament into Greek and from that into Latin. Allen^{1b} states: "It contributed more to the liberation of the human mind from the thralldom of the clergy of that day than all the uproar and rage of Luther's pamphlets." His book "In Praise of Folly," is still being reprinted after 500 years. It pointed out the foibles and weaknesses of many professions—particularly the clergy, the law, and the medical profession. Thus he speaks of the medical profession of his day in commenting on naturalists, astrologers, and logicians: "While all these hard named fellows cannot make so great a figure as a single quack, and in this profession, those who have most confidence, although the least skill, shall be sure of the greatest custom; and indeed, this whole art as it is practised now is but one incorporated compound of craft and imposture." Erasmus once wrote⁴: "The Art of Medicine I have never learned." Physicians used astrology and the supernatural; for example, syphilis was blamed on the conjunction of the planets. Lindeboom⁴ tells us that Linacre, one of the founders of the College of Physicians, sent to Budaus, the first Greek scholar of the age, a gold ring and 18 silver rings blessed by Henry VIII as a preservative against convulsions. In a letter⁴ he describes with much sarcasm a consultation of

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Prof. E. E. Ecker of the Institute of Pathology, Western Reserve University, Medical Department, translated the Dutch articles quoted in this study.

Read before the Section on Dermatology and Syphilology at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 14, 1951.

1. (a) Hilton, J.: "The Unequal Marriage," with Biography, *Am. J. Surg.* 40: 491, 1938. (b) Allen, P. S.: Desiderius Erasmus, in *Encyclopaedia Britannica*, ed. 11, New York, Encyclopaedia Britannica, Inc., 1910, p. 721.

2. Allen, P. S.: Erasmus, New York, Oxford University Press, 1934.

3. Smith, P.: Erasmus, New York, Harper & Brothers, 1933.

4. Lindeboom, G. A.: *Erasmiana Medica*, Nederl. tijdschr. v. geneesk. 80: 3164, 1936.

12 physicians concerning a very sick man. They all agreed that he would die; they all suggested an autopsy and then demanded their separate fees. Erasmus' "Adagia" ² went through some 60 editions in his lifetime and 75 more in the 17th century. Erasmus was especially noted for his correspondence. Almost all portraits show him at a desk with pen in one hand and his small cup of writing fluid in the other. He would write as many as 40 letters a day, which covered all phases of the life of the period—methods of trade, the home, the town, the dangers from disease, violence, social pressure, education, and lack of education for women. He stressed the difficulties of travel, which was mostly by boat, horseback, and more rarely by a two or four horse coach. He deplored uncleanness and rat and bedbug infested inns, where two, three, or four travelers would be put in one bed. Moreover, roads were not safe because of robbers and knights who would rush out from their castles to "exact toll." There were frequent flare-ups from the plague in the rat- and flea-infested inns, boats, and houses. Erasmus depicted such a place in "Stamm Room," a crowded inn, with foul air and dirt. Frequent blasts of flatus could be heard, and, finally, when your host would allow you to sit down, beer, or some vile wine, and fish would be your meal—a well fried, possibly cold German carp. The guests remained seated until 10 p. m., and then went to bed with two or three bedfellows.

ERASMUS AS HYGIENIST AND PHYSICIAN

While Erasmus was, himself, the product of an unwed mother and father, he did everything possible to correct this situation for others.¹ On the value of the proper marriage, he wrote "The Suitor and The Maiden" and "The Unhappy Wife," on the intelligent education of the son, "The Lying in Woman," and on venereal disease, "The Young Man and The Girl" and "The Un-Marriage." He emphasized sexual promiscuity and venereal disease. In "The Young Man and The prostitute" he depicts the prostitute as an open cloaca, into which dirty, impure, diseased men come together. Erasmus, 500 years ago, advised all mothers to nurse their babies and not to have wet nurses. He was appalled at the spread of syphilis and emphasized the danger of a syphilitic man to a healthy wife. He stated that if he were the Pope, though the marriage had been bound with 600 marriage contracts, he would still render it void. He warned of the dangers of kissing, of using unsanitary drinking utensils, and of hiring unclean barbers. He said that guests in inns should demand clean, fresh linen and concluded that cleanliness was essential for health. One should not stay in an unventilated room, he should shave himself, and he should not use adulterated wines. Barbers should not try to be surgeons.

DISEASES OF ERASMUS

While he was a young boy in Holland ⁵ he had an attack of quartan malaria, which occurred occasionally for years. He suffered from renal and, later, vesical calculi, which troubled him the rest of his life. A Hungarian physician ⁶ sent him an astrological pitcher, or china hot water bottle, in the shape of a lion. It relieved him but he could not understand the significance of the lion. He had stomach upsets from time to time, especially when on a journey and when he was forced to eat fish. His remedy for the trouble was to stick his finger down his throat until it was "successful." As he got older, he was troubled with gout and, at times, with dysentery. The last was probably a result of flies, lack of refrigeration, and general uncleanness. Because of his "arthritis," he preferred an open fireplace, and frequently moved to escape cholera or the plague—both of them being frequently observed. In August, 1514, he had attacks of spitting. Some physicians considered Erasmus as a hypochondriac and neurotic.⁷ Schenk ⁷ examined his letters and concluded that Erasmus was a man of an emotional, volatile nature, and that he was psychasthenic. Erasmus undoubtedly deplored his origin, and went to the Pope to have it remedied. He could not stand contradiction, but was himself a man of contradiction.⁸

In October, 1518, he recovered from a long sickness. He wrote to Beatus Rhenanus ⁸ concerning a trip from Basel to Louvain—partly by boat, partly by horseback, and partly by covered wagon. In an inn he ate codfish, which made him ill, and a skin eruption developed, with swelling of the nodes in the groins and with lesions under the left buttock. After two days' riding it became worse and burned, and high up on the left groin a hard node appeared, but it produced no pain. Erasmus did not think he had the plague. The horseback ride irritated the kidneys, so that he could not walk, and cold air aggravated the pain. Then he hired a covered wagon with four horses. The abscess in the groin broke, and the pain was better. He had no stupor or emesis. One physician applied compresses, but a third swelling started after rose oil was rubbed over the kidneys. The physician then told a servant that the patient had the plague. Another physician advised a urine examination, and suspected furuncles. One other, in Louvain, told him he had a bad swelling in the nodes. Erasmus gave him a gold coin, and the physician left and sent his servant the next day. After 17 days, black dead flesh came from the boils—the one in the left groin being the last to heal. A swelling of the left breast then developed, but it receded gradually. Feis ⁹ thinks Erasmus had the bubonic plague in a mild form. Essed ¹⁰ wonders if it might have been *frambesia tropica*, brought to Europe from the Far East by the Portugese. He recovered, as far as we know, and returned to Basel. Some think this was an unusual infection with syphilis. Certainly, severe furunculosis or lymphogranuloma would have to be considered.

Erasmus remained in Basel for the remainder of his life, except for a period of several years spent in Freiburg in Alsace at the height of the Reformation Movement. He preferred to remain neutral in this struggle. He was active in writing, editing, and letter writing, until his last illness, when he contracted dysentery, one of his old

5. Nuyens, B. W. T.: Geschiedenis der Geneeskunde, Nederl. tijdschr. Geneesk., 80:3157, 1936. Noury, P.: La Santé d'Erasmus, Chron. méd., 12:165, 1936. Lindeboom.⁴

6. Braun, A.: Generative Ethik vor 400 Jahren, München. med. Wehn., 81:681, 1934.

7. Schenk, V. W. D.: Erasmus' Character and Diseases, Nederl. tijdschr. Geneesk., 91:702, 1947.

8. Lindeboom, Schenk.⁷

9. Feis, O.: Die letzte Erkrankung des Erasmus von Rotterdam, Deutsche Arch. Klin. Med., 135:56 and 371, 1921.

10. Essed, W. F. H.: Over den Oorsprong der Syphilis, Diss. Amsterd., 1922.

complaints, along with uremia, and died, July 22, 1536, aged 70, in the home of Frobenius, son of Johann, the famous printer. In his last hours, Dutch, his mother tongue, came back to him as his last words. He died² without attendance of the church. In his will, filed Feb. 12, 1538, with the exception of some legacies to Amerbach, his property was all given to the aged and infirm, to young girls, and to young men for their education. There were no legacies for masses or other clerical purposes. Erasmus was buried in the middle nave of the Basel Münster, and the site was marked by a marble epitaph, placed Oct. 30, 1538, by his friends Bonifazius Amerbach, Hieronymus Froben, and Nikolaus Epicopus.

In June, 1928, his burial site was opened, owing to the construction of a new system of central heating. After some difficulty in finding the skeleton, it was definitely located in a deep site in the sand and gravel. Werthemann,¹¹ now professor of pathology at the University of Basel, was able to show, without any doubt, that the skull was that of Erasmus.

In the Institute of Pathology of Basel exhaustive study was made of the entire skeleton, which was in a remarkable state of preservation after 500 years. The height was estimated at 173 cm. (5 ft. 8 in.); the skull was small, with a capacity of 1,255 cc. (brain capacity 1,200 gm.). The average Caucasian and Chinese skull is 1,300 gm. The left tibia and left ulna revealed some unusual changes. The left tibia was 5 mm. shorter than the right, and the left ulna was 8 mm. shorter than the right. Just below the middle of the shaft of the left tibia, on the anterior border, there was a hard, bony proliferation

9 cm. long. The same was true of the left ulna in the lower quarter, and it was of the same type. The bone in the affected area was thickened and porous. Studies of the decalcified bone from these areas showed on staining with hemalum, that the thickening was periosteal in type. The author, from his exhaustive study, concluded that it could only be syphilis. Furthermore, in this type of syphilis the borderline between diseased and normal bones is sharp, and such was found to be the case here. Werthemann found no evidence of congenital syphilis. Erasmus' teeth, especially the upper central incisors, were in a remarkable state of preservation. Werthemann's diagnosis was osteitis and periostitis syphilitica acquisita. Werthemann thought of the possibility of Erasmus' having contracted syphilis in his journey to Louvain. Moreover, Werthemann mentions the pandemic type of syphilis seen in the latter part of the 15th century and in all of the 16th century. It may have been an asymptomatic infection, which we now recognize as far from rare. But in Erasmus' time there was an epidemiological picture much similar to that portrayed by Jessner¹² and his colleague in Asiatic Russia in 1928. Is it possible that some of Erasmus' arthritis was an old syphilitic osteoperiostitis?

1352 Hanna Bldg.

11. Werthemann, A.: Schädel und Gebeine des Erasmus von Rotterdam, Verhandl. d. naturforsch. Gesellsch. 40: 313, 1930. Pfister, C. R.: Zur Krankheit des Erasmus, Schweiz. med. Wchnschr. 66: 846, 1936. Editorial, Lancet 215: 1300, 1928.

12. Jessner, M., and Rossiansky, N.: Die Ergebnisse der deutsch-russischen Syphilis-Expedition, 1928, Arch. f. Dermat. u. Syph. 160: 224-225, 1930.

WOMEN IN MEDICINE

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With the demand for more doctors and the obvious difficulty in expanding training facilities rapidly, a study of the effectiveness of women in medicine was deemed timely. The investigation was designed to determine to what extent women physicians utilized their training in their communities and within their profession. It was hoped also that the findings might prove of value for student counseling during college and premedical training as well as during the undergraduate medical years.

Very little attention has been given to determine how effectively any physician's time is utilized after graduation. There is therefore no available study of medical manpower with which to contrast these findings. In this limited undertaking the main comparison or the most obvious one that might prove of value was between the careers of the unmarried and those of the married women. This comparison is really not just. It might be more logical to compare unmarried women with male physicians. It should be self-evident that there are problems with which the married professional woman has to deal that are outside the sphere of either the male or the unmarried professional woman. The married woman has

two jobs, but the primary one should be the maintenance of a family unit and the rearing of the young. The woman is the integral part in homemaking. No matter how great recognition a professional married woman attains, she will not be considered a success if she has failed in her home. Does success necessarily mean a high rank in a university, in a hospital, or in medical societies? If a married woman physician can make a valuable contribution to health while rearing a family, may not this represent an equivalent accomplishment?

The problems peculiar to the married professional woman should be viewed realistically. First, she does not select her location but follows her husband. Locating herself is secondary to the establishment of her husband in his career. She must create her opportunity in the environment in which she finds herself, which may limit her as to the type of work available, the time that can be devoted to it, and the remuneration. In other words, she does not have full choice in deciding what she is best fitted to do.

This study was made under the auspices of the Dr. Wansa Fund of the Women Physicians' Club of San Francisco.

Second is the problem of children. The ultimate of any marriage is the production of offspring. The number of children in the group studied compared favorably with that in other educated groups, which would indicate that these women have a sense of responsibility in this regard. The bearing of the child and the nurturing of it through

TABLE 1.—Medical Education and Certification of Women Physicians by Year of Graduation

Medical Education, Training, Certification	Decade of Graduation			
	Total, %	Before 1900, %	1900-1909, %	1910-1919, %
Total.....	100	100	100	100
Premedical education.....	81	82	85	89
Internship.....	81	85	82	84
Residency.....	72	80	79	80
Certification by specialty boards.....	45	49	42	45

early infancy, however, takes energy, devotion, and time which must be subtracted from a career.

Third is the problem of competent household help and the attendant expense. The woman physician—in fact, any working woman who is a housewife and mother—must of necessity have competent help. At present this cost cannot be deducted from the income tax. This undeductible expense virtually forces some women out of practice.

Fourth, probably the most difficult problem is that of maintaining contact with the medical field during periods of home responsibility, or of refreshing one's training after the homework has diminished. It is almost impossible for the married woman physician to get any appointment to complete her training, to refresh herself after a period of inactivity, or to find part-time jobs when she cannot be fully employed.

The question logically arises: Can women physicians make any especial contribution to medicine because they are women? If they can, this would seem to be justification for both men and women to help these physicians surmount the difficulties encountered.

Statistically, women constitute over half of the population. Can knowledge of their physical and emotional needs be enhanced by the interpretations of scientifically trained women who have also had personal experience? Much of the life of the female poses problems distinctly

TABLE 2.—Percentage of Women Physicians Single and Married According to Medical Education and Training and Certification by Specialty Boards

Status	Total, %	Training and Certification			
		Premedical Educ., %	Intern- ship, %	Resi- dence, %	Specialty Certifica- tion, %
Single.....	50.100	78	79	78	49
Married.....	49.900	80	81	80	47

different from those of the male. Thus from the age of 9 to 13, when a boy can cheerfully not only mock the doctor's rules but also Kinsey's, the girl must learn to contend with menstruation, the hygiene of it, the limitation it imposes, and the hazards it bears.

The young adult female experiences pregnancy; the anatomical, physiological, and psychological alterations accompanying it; delivery; and lactation. In addition, some will experience abortion, abnormal delivery, or

trauma to the organism. Others experience the distress of sterility or at times are blamed even for producing the undesired sex of the offspring.

The full and extremely important period, when children are little and dependent, comes to an early end, and the middle-aged woman must adjust to the void left by the departure of her children, the consequent leisure with which she is not prepared to deal or to utilize properly. She usually outlives her husband and in old age must make a final adjustment to another complete change in her way of life. These areas in a female's life should be enriched by the contributions of women scientifically trained and personally experienced. Related intimately, also, to a woman's world are community activities, such as health education, school health, recreation, delinquency, social and economic pressures, and prejudices. All of these are more often the concern of women in the roles of wives and mothers than of men. In fact, all of medicine might gain materially from a feminine as well as a masculine point of view.

The analysis of women physicians as to the competency of their training, motivations to enter medicine, the

TABLE 3.—Teaching and Research Appointments Held by Single and Married Women Physicians According to Time of Graduation

	Total, %	Decade of Graduation		
		1900-1909, %	1910-1919, %	Before 1900, %
Single Women Physicians				
Total.....	(74) 100	(24) 100	(27) 100	(23) 100
Teaching appointments...	55	34	38	53
Research.....	31	22	33	29
Married Women Physicians				
Total.....	(120) 100	(57) 100	(40) 100	(23) 100
Teaching appointments...	42	31	30	43
Research.....	15	19	5	15
All Women Physicians				
Total.....	(200) 100	(80) 100	(67) 100	(50) 100
Teaching appointments...	48	37	32	48
Research.....	20	22	13	20

use that has been made of the training, and the differences that marriage has made is the subject of this paper. The complete study will be reported in the *Journal of the American Medical Women's Association*, in order that any other group contemplating a study of medical manpower might have the benefit of our experience.

The study was made under the directorship of Eschscholtzia L. Lucia, Ph.D., a consultant in medical biometry, who was assisted by Helen C. Ferris, A.B. The group of women physicians studied comprised those in the San Francisco Bay Area, including the counties of Alameda, Contra Costa, Marin, San Francisco, and San Mateo. Returns were completed from 230 of 394 schedules sent out. Thirty-two per cent of the responses (74) came from single women and 68% (156) from married. The training of these women is given in Tables 1 and 2.

The general trend toward better premedical education and postgraduate training is obvious and reflects a general trend in all of medical training. By graduation decades, there is an increase in the percentage of women who received premedical education from 69% to 86% to 92%. The percentage increase in residencies is even more marked: 55% in 1930 versus 82% in 1940. Similar differences are seen with respect to certification of specialty board, for, even among the women physicians

who graduated in 1940 or later, 19% are or have pending certification. Forty per cent of single women were certified. For the total group the figure was 25%. Even without over-all figures for comparison, the study would seem to indicate that women do seek and obtain good training.

In addition to training, it would be desirable to determine the participation of women in teaching and research.

Of the 74 single women, 41 (55%) are reported as having held teaching appointments, while, among the 156 married women, 66 (42%) so reported. Twenty-three, or 31%, of the single women have held research appointments, and 23, or 15%, of the married have held such appointments.

The single women's scientific achievements exceed those of the married women. When classified according to graduation decades, in the original tables the percentage of single women who held either teaching or research appointments were higher in every instance save one. Although none of the differences between the per-

TABLE 4.—Medical and Scientific Achievements of Single and Married Women Physicians as Indicated on Questionnaire

QUESTIONS			
1. Do you belong to medical and/or scientific societies?			
2. Have you been elected to honor societies?			
3. Have you actively participated in societies?			
4. Have you published medical and/or scientific papers?			
5. Have you held teaching appointments?			
6. Have you held research appointments?			
	Single Women, %	Married Women, %	
Total	(74) 100	(156) 100	
Total answering in affirmative.....	(72) 97	(134) 86	
All 6 questions.....	6	1	
5 questions.....	16	4	
4 questions.....	22	10	
3 questions.....	12	24	
2 questions.....	19	22	
1 question.....	22	25	
All questions answered in the negative....	3	14	

centages of single and married women is statistically significant as judged by the limits imposed, the consistencies of results showing that single women in each graduation decade participated to a greater extent should give credence to the conclusion that they are more active in teaching and research than their married contemporaries. The medical and scientific achievements of the single women reporting far exceed those of the married women. The difference in total achievement is statistically significant.

In order to determine the use that is made in professional services to the community, Table 5 indicates the division into specialties.

Ninety-one per cent of the single women physicians practice medicine full time, as compared with 75% of the married women physicians. Thirteen per cent of the married women were engaged in part-time medical activities, while none of the single women were occupied solely in part-time medical activities. Many of the 67 single women reporting full-time work in medical fields for which they were trained gave time to more than one medical activity, such as participation in institutional work, hospitals, and clinics in addition to their practice. Among the 118 married women reporting full-time medical practice, there were some who were interested also

in additional medical activity, such as part-time work in hospitals, institutions, and clinics or other community activity.

Forty-two per cent of the women physicians reported that they were engaged in full-time private practice of a specialty. Approximately one-third of the specialties were

TABLE 5.—Types of Practice in Which Single and Married Women Were Engaged in 1949-1950

Type of Practice	Total, %	Single, %	Married, %
Total	(230) 100	(74) 100	(156) 100
Full time	80	91	75
General practice	15	15	16
Specialties	42	62	33
Institutions, hospitals, and clinics	13	11	14
Residencies	3	5	1
Public health	7	8	6
Part time	8	0	13
Retired	2	1	2
Not practicing	10	8	10

in pediatrics; 13% were in psychiatry, medicine, and obstetrics and gynecology, respectively; 6% were anesthesiologists; and 4% were radiologists. The remaining 19 were engaged in the practice of 12 other specialties. This high percentage of women specializing may mean that there are better opportunities for women in the specialties, that possibly there is less prejudice against them in some of the specialties, or that regular work in a specialty may be better suited to married life.

In order to determine the effect of marriage on a career, a study of the time of marriage, the completion of training, and the time and number of children was made. The results are reported in Tables 6 and 7.

The time of the first change of marital status for 154 women who were married and reported is as follows: Nineteen (12%) were married before entering medical school, 33 (21%) while attending medical school, 47 (31%) during graduate training, and 55 (36%) after beginning their careers in medical and health activity.

TABLE 6.—Relation Between Time of First Marriage of 99 Women and Time of Beginning a Family According to Periods in Medical Education and Career

Time of First Child *	Time of Marriage				Total
	Pre-medical Years	While Attending Medical School	During Graduate Training	After Attaining M.D.	
Premedical years.....	4	..	..	..	4
Attending medical school	2	5	..	..	7
During graduate training	4	7	10	..	21
After attaining M.D.....	0	9	26	30	65
Total.....	10	21	36	30	97 †

* Including adopted children.
† Two women reporting children and who were married during their premedical years did not give the time of adoption of their children.

Of the 10 women who married during their premedical education, all had children before attaining the degree of M.D. Among the 21 women who married while attending medical school, 9 (43%) waited until after receiving their M.D. degrees before having children. Among the 36 women married during graduate training, 26 (72%) waited until after receiving their degree. Approximately one-third of the first marriages occurred before completion of premedical and medical education,

one-third during graduate training, and one-third after the degree of M.D. was received. In comparison, two-thirds of the first children were born or adopted after their mothers had received the M.D. degree.

Ninety-two women who had spent the time required to become licensed physicians also had families with

TABLE 7.—Families Classified According to Number of Children and Birth Decade of Mother

No. of Children	Total Women	Decade of Birth of Mother			
		1915-1924	1900-1914	1885-1899	Before 1890
None	57	21	23	10	3
1	32	14	11*	6	1
2	40	10	17†	9†	4
3	19	7	7	3†	2
4	6	1	3†	..	2
5	2	..	1	..	1
Total.....	156	53	62	28	13

* Four families with no children of their own adopted a total of 7 children.

† Six families with children of their own adopted a total of 10 children.

children, either their own or adopted. Ninety per cent of the families of the 99 women were comprised of their own children, 4% of their families were adopted children only, and 6% of their families were both their own and adopted children. Ninety-five women physicians reported having borne 188 children, an average of approximately two children for each woman. Seventy-nine (51%) reported that they had married physicians. The next highest group of husbands followed other professional or technical occupations.

Among the 74 women who had never married, only 10 (14%) reported periods of inactivity in medicine and other health activities. The periods of inactivity were attributed to a number of reasons, such as ill health, care of children, psychoanalysis, study, and travel. All periods of short duration except for one, which was over years. On the other hand, among the women who married, there were 73 (46%) who reported periods of inactivity. The reasons for the inactive periods for married women are given in Tables 8 and 9.

It is estimated statistically that the total time lost in the practice of medicine of the married woman is equal to over 40 years of the practice by each of four medically

TABLE 8.—Periods of Inactivity Among the Married Women Classified According to Types of Medical Work

Type of Medical Work (1919-50)	Total	Less than 1 Year	1-5 Years	Over 5 Years
Specialties	25	14	6	5
General medicine	8	3	3	2
Hospitals, clinics, institutions	9	4	4	1
Public health	2	2	..	..
Professional work	29	1	16	9
Total.....	73	27	29	17

trained persons. The minimal approximation of time lost by the single women was computed by utilizing the same median and the minimum number of years as for the married women. This time lost is equal to one-half of a professional life of 40 years of one person. Ten women were responsible for the loss of approximately 20 years.

The analysis of motivations reveals that family tradition still exerts considerable influence on the women who enter the profession. Forty-six per cent reported early

medical family contact. Practically all the women physicians reported that they had retained their interest in medicine whether or not they were actively engaged in it as a profession.

The activities of these women in community projects indirectly related to the medical field, such as Red Cross and health committees, were not studied. It would be interesting to see whether the married woman physician has turned to these activities when she has been unable to find an outlet in the medical field. Even in such a capacity she might render very useful health services.

CONCLUSIONS

Even without the possibility of comparing this study with a similar one for all medical manpower, it is obvious that the great majority of women work hard at being good physicians and, by the selected standards, succeed. It would be interesting to know the comparison with men on such matters as certification, participation in scientific activity, types of practice, and, particularly, time out from practice. The single women probably would compare favorably with the men. Such a study of medical manpower might be profitable at this time.

TABLE 9.—Reasons Given for Periods of Inactivity Classified According to Type of Medical Work

Type of Medical Work (1919-50)	Total	Pregnancies	Home and Children	Travel	Illness	Other	None
Specialties	25	13	5	3	2	2	..
General medicine	8	4	..	..	2	2	..
Hospitals, clinics, institutions	9	3	2	..	2	..	2
Public health	2	1	1	..	..	..	..
Part-time or no professional work	29	18	5	..	5	1	..
Total.....	73	39	13	3	11	5	2

It would be highly desirable, in order to interpret health, male and female, more accurately, to have a higher percentage of women trained in medicine. In many of the European countries, where women's place in medicine is accepted with greater realism, the percentage reaches 20 to 25.

Careful thought and study should go into the selection, training, and timing of the training of women in order to reduce time lost to active health work.

Inventory should be made of community health activities particularly suitable for women physicians during the interval when they must devote much time and energy to the rearing of children. There are many important health jobs difficult to fill, because they are part-time or nonremunerative, for which married women rearing a family would be ideally suited.

Women who have had to take time from medical activity to rear a family should be given the opportunity to return for refresher courses in medicine or residency training if desired.

Since medicine is a demanding profession, careful counseling of girls contemplating premedical and medical courses is urgently needed. Counselors should be aware of the problems with which married women physicians are confronted, and they should have available the analysis of types of work suitable for the period of child-rearing in order to help girls plan their training.

A change of attitude with more realism and understanding of the married women physicians' problems would materially decrease the period of inactivity or the abandonment of the work entirely by the medically trained woman.

For all working women the problem of tax relief for household help should be given consideration and promotion by interested groups.

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CLINICAL NOTES

FATAL HEPATIC NECROSIS OCCURRING DURING THERAPY WITH PHETHENYLATE SODIUM

REPORT OF TWO CASES

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and

H. Stephen Gallager, M.D., Philadelphia

Two cases of fatal hepatic damage in patients receiving phethenylate ("thiantoin") sodium are reported, and the possible hepatotoxic effect of this drug is discussed. In both patients, a 44-year-old woman and a 6-year-old boy, there was no evidence of infectious disease when the acute hepatic failure developed. Both had been receiving phethenylate for about five months for the control of convulsive seizures, and, while homologous serum hepatitis cannot be excluded definitely, it appears that the phethenylate contributed to the development of the disease.

REPORT OF CASES

CASE 1.—M. C., a 44-year-old white woman, was admitted to Germantown Hospital on May 25, 1950, complaining of jaundice. She had been taking phethenylate sodium, 0.2 gm. three times daily, for five months for control of petit mal seizures. Sixteen days before admission nausea and anorexia developed, and two days later vomiting occurred. On May 23 she first noted jaundice, dark urine, and clay-colored stools. At the time of admission her temperature, pulse, and respiratory rate were normal. The liver was not palpable, and there was no abdominal tenderness. The urine contained bilirubin, but no urobilinogen. The prothrombin time was 28.5 seconds (control time 16.8 seconds), and the alkaline phosphatase value was 10.2 Bodansky units. The reaction to a cephalin flocculation test was 4+ in 24 hours. The blood urea nitrogen level was 5 mg. per 100 ml., and the total plasma cholesterol level was 157 mg. per 100 ml., with 17 mg. per 100 ml. as esters.

On the third day of hospitalization the patient had sudden massive hemoptysis. No local bleeding points were found in the nose or pharynx. Two days later she had become confused and somnolent and by the seventh day she was deeply comatose. She died on the eighth day of hospitalization. Terminally her temperature rose rapidly to 105 F. Permission for autopsy was not granted.

CASE 2.—G. H., a white boy aged 6 years, had had frequent convulsive seizures since birth. In June, 1950, after adequate neurologic study in a metropolitan medical center, the administration of 0.12 gm. of phethenylate sodium twice daily and 0.015 gm. of phenobarbital three times daily was started. The attacks were controlled, and the child entered grade school in September, 1950. About Nov. 14 the patient's mother first noticed that he was listless, and within a few days jaundice, dark urine, and pale stools appeared. With the onset of these symptoms, phethenylate

was withdrawn and phenobarbital was reduced to two doses daily. On the advice of a physician, he was confined to bed at home and treated expectantly. The symptoms were progressive and on Dec. 3 he became excessively irritable. The following day the mother, recognizing what she believed to be the prodromata of a convulsive seizure, administered secobarbital (seconal®) sodium, 0.05 gm., by mouth. The child shortly fell into a deep coma from which he could not be aroused. He was admitted to Germantown Hospital on the following day.

On admission, he lay in a flaccid state, deeply comatose and deeply jaundiced. Some tiny fresh lacerations were noted at the edges of the tongue. The liver was not palpable. The pulse and respiratory rate were rapid, and the temperature was 99 F. The serum bilirubin level was 19.8 mg. per 100 ml., the icterus index 108. The serum protein value was 4.7 mg. per 100 ml., and the reaction to a cephalin flocculation test was 4+ in 24 hours. The spinal fluid was chemically and morphologically normal.

Respiratory difficulty appeared and increased during the night. The day following admission, inspiratory sternal retraction and crowing respirations were prominent. Neither intravenous administration of calcium gluconate nor tracheotomy resulted in improvement and the patient died 15 hours after admission.

At autopsy, the liver was found to be soft and friable, with a mottled yellow and pink surface. It weighed 430 gm. A large cavity, presumably the result of a resolved hematoma incident to birth trauma, replaced the anterolateral two-thirds of the left cerebral hemisphere. Except for scattered areas of atelectasis in both lungs, the remaining viscera were normal. Sections of the liver showed massive diffuse necrosis of parenchymal cells and replacement by reticulum and young fibrous tissue. There was only a sparse scattering of inflammatory cells. No hepatic regeneration was evident, nor was there significant proliferation of bile capillaries. In general, on microscopic examination the liver resembled histologically a liver with acute fulminating hepatitis of virus origin.

COMMENT

Phethenylate sodium is chemically sodium 5-phenyl-5(2-thienyl) hydantoinate, and thus is structurally related to both diphenylhydantoin (dilantin®) sodium and mesantoin® (3-methyl-5,5-ethylphenylhydantoin). Hepatic damage owing to both of these agents has been reported,¹ and it is not unreasonable to assume that a related substance has similar toxicity. Few reports of reactions to phethenylate² have been published and they are concerned largely with effects on the skin and the hematopoietic system. These reports indicate at least that phethenylate is not entirely innocuous. While the two cases reported here cannot be regarded as conclusive evidence that phethenylate is a hepatotoxic material, several factors suggest this possibility.

Certain similarities in the clinical evolution of the two cases are striking. Both patients had received the drug for about five months; acute hepatic insufficiency developed in both without evidence of systemic infectious disease. Neither had an elevated temperature until the last few days of life. From a more negative standpoint, it must be noted that the two cases originated in separate localities at different times. Infectious hepatitis was not unusually prevalent in the vicinity at the time either case occurred.

From the Departments of Pediatrics and Pathology, Germantown Dispensary and Hospital.

1. Chaiken, B. H.; Goldberg, B. I., and Segal, J. P.: Dilantin Sensitivity: Report of Case of Hepatitis with Jaundice, Pyrexia and Exfoliative Dermatitis. *New England J. Med.* 242: 897-898 (June 8) 1950. Kozol, H. L.: Mesantoin® in Treatment of Epilepsy: Report of 200 Patients Under Treatment for Periods Ranging from Two Months to Four Years. *Arch. Neurol. & Psychiat.* 63: 235-248 (Feb.) 1950.

2. Weiss, H. A., and Hawley, W. D.: Pancytopenia Following Use of Mesantoin and Thiantoin: Report of Fatal Case, U. S. Armed Forces M. J. 2: 83-86 (Jan.) 1951. Best, W. R., and Paul, J. T.: Severe Hypoplastic Anemia Following Anticonvulsant Medication: Review of Literature and Report of Case, *Am. J. Med.* 8: 124-130 (Jan.) 1950.

On the other hand, the possibility of needle-borne hepatitis cannot be excluded. Both the patients had had intensive diagnostic studies, five months and six months, respectively, before the onset of the symptoms, and at that time undoubtedly had been subjected to venipuncture. In Case 2 phenobarbital was given concomitantly, and while it is authoritatively stated that "hepatic function is unimpaired by therapeutic doses of barbiturates,"³ such reactions apparently may occur occasionally in sensitive persons.⁴ Case 2 illustrates also the danger of administering barbiturates in the presence of severe liver damage. There seems to be no doubt that in this instance the immediate cause of death was barbiturate intoxication, resulting from the inability of the damaged liver to destroy secobarbital.

It would be decidedly unfair, on the basis of the evidence presented, to condemn as dangerous an otherwise valuable therapeutic agent. Such reactions as have been described seem to occur in especially predisposed persons, and it is probably feasible to use phethenylate with impunity in the average person, even on a long-term basis. Further study is obviously necessary to determine whether phethenylate is a hepatotoxic agent. It is hoped that this report will stimulate investigation to that end.

SUMMARY

Two fatal cases of hepatic failure in patients receiving phethenylate ("thiantoin") sodium therapy are reported. Indirect evidence indicates an etiologic relationship between disease and the drug, although homologous serum hepatitis cannot definitely be excluded. The need for intensive study of the problem is recognized and investigation urged.

East Wister St. (Dr. Gallagher).

3. Goodman, L. S., and Gilman, A.: *Pharmacological Basis of Therapeutics*. Textbook of Pharmacology, Toxicology and Therapeutics for Physicians and Medical Students, New York, The Macmillan Company, 1955, p. 135.

4. Weiton, D. G.: Exfoliative Dermatitis and Hepatitis Due to Phenobarbital, *J. A. M. A.* 143: 232-234 (May 20) 1950.

ACUTE HEPATIC NECROSIS WITH DEATH OCCURRING DURING PHETHENYLATE SODIUM THERAPY

REPORT OF TWO CASES

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Phethenylate ("thiantoin") sodium or "thyphenytoin" (5-phenyl-5-[2-thienyl] hydantoinate) was first prepared in 1941. The initial clinical results, however, were not published until 1948, when Peterman¹ reported on a series of 73 children with convulsions who were treated with the drug for two years. His results indicated that phethenylate was effective in controlling both grand mal

and petit mal seizures. The toxic side-reactions were relatively insignificant and consisted of hyperplasia of the gums, ataxia and incoordination, and rash. In 1950 Carter and Merritt² reported that phethenylate sodium was ineffective in treatment of petit mal seizures.

We have treated 153 patients with phethenylate over a period of three years. We observed that the drug was somewhat effective in the control of grand mal seizures, but was not appreciably beneficial in treatment of petit mal and psychomotor seizures. In addition to the untoward reactions reported by Peterman, jaundice has been noted by us in three patients and has also been reported by others.³ Two of our patients died of fulminating hepatitis while taking this drug. The purpose of this paper is to report the clinical and pathological findings in these two cases.

REPORT OF CASES

CASE 1.—E. T., a 39-year-old white man, was admitted to the Johns Hopkins Hospital on Feb. 27, 1950, with a chief complaint of convulsions of 25 years' duration. At the age of 14 the patient had his first generalized convulsion, and he continued to have similar convulsions on the average of once every three months up to the time he was first seen by us. He had been treated with phenobarbital and diphenylhydantoin (dilantin[®]) sodium without benefit. The history revealed that the patient had had an exploratory craniotomy in 1928 at another hospital. There was no family history of epilepsy or allied disorders.

Physical examination revealed a tall, thin, white man in no acute distress. The temperature, pulse rate, respiration rate, and blood pressure were normal. There were multiple traumatic scars over the face, trunk, and extremities and a large, irregular defect of the vertex of the skull about 12 cm. in diameter. The dura could be felt easily and was thought to be thickened and possibly partially calcified. The neurological examination disclosed no abnormalities.

A roentgenogram of the skull revealed a very large operative defect extending from the right side of the skull about 4 cm. above the level of the sella turcica, across the midline, and about 3.5 cm. into the left parietal region. The right lateral two-fifths of the defect was covered by a bone flap; the central portion of the defect showed no bone flap or other covering. An electroencephalogram showed moderately abnormal waves, slow and fast for age, with spike and wave seizure bursts produced by over-ventilation. Results of serologic tests for syphilis were negative. The blood and urine were normal. The patient was discharged on the fourth day of hospitalization, with instructions to continue phenobarbital as before (0.1 gm. three times daily) and to take phethenylate sodium 0.13 gm., three times daily.

During the following six months the patient continued to have seizures as before, in spite of increasing the dose of phethenylate sodium to 0.26 gm. three times daily. He also complained of irritability and of not feeling "quite up to par." He was seen by one of us (S. L.) on Aug. 14, 1950; at this time he was very tired and somewhat drowsy, but examination revealed no abnormality. He was advised to continue therapy. The next day he felt exhausted and complained of back pains and a pressing feeling over the upper abdomen; he tended to sleep most of the time. The following day, Aug. 16, his sister, a registered nurse, noted a yellow tint in his scleras. In the following three days he became increasingly jaundiced and drowsy. The temperature was subnormal and he sweated profusely. Bowel movements were clay-colored and the urine very dark. He complained of nausea once. There had been no constipation, diarrhea, or vomiting. On Aug. 19 he became delirious and was brought to the hospital for admission.

Physical examination revealed a temperature of 99 F, a pulse rate of 120, and blood pressure of 135/50 in both arms. He was a lean, muscular, markedly jaundiced, mildly delirious, white man with fetor hepaticus. There were rhythmic tremors around the mouth and an occasional coarse tremor involving the entire right arm. Scattered musical rales were heard at the bases of both lungs. Examination of the abdomen revealed no abnormality.

The microphotographs shown were made by Miss Joan Wheaton. The clinical and necropsy material concerning the patient in Case 2 was supplied by Drs. Philip F. Lerner and John A. Wagner. From the Departments of Pediatrics and Pathology, Johns Hopkins University Medical School, and the Epilepsy Clinic, Johns Hopkins Hospital.

Neurological examination showed all deep tendon reflexes to be hyperactive, with transient suprapatellar and ankle clonus bilaterally.

The clinical impression was that the patient had acute yellow atrophy of the liver owing to an unknown toxic agent or infectious hepatitis. He was treated symptomatically, but rapidly became moribund, never regaining consciousness. He died three days after admission.

At autopsy (performed by Dr. Albert Shackman) the body weighed 67.5 kg. The scleras were icteric and the conjunctivas appeared edematous. The mouth contained dried blood. The left thigh measured from 2 to 3 cm. larger in circumference than the right at the same level. A 12 cm. oval defect was observed in the calvarium at the site of the previous operation. In addition, there were several other healed scars on the abdomen and extremities.

The abdomen contained about 1 liter of icteric fluid. Each pleural cavity and the pericardium contained 100 cc. of similar fluid. Grossly, the heart appeared normal (weight 340 gm.) except for the icteric color of the valves. There were numerous subpleural petechiae of the lungs. The upper lobe of the right lung appeared consolidated, and to a lesser extent, the lower lobe. The tracheal and bronchial mucosa was red. The liver appeared small (1,150 gm.) and pale, with a wrinkled capsule. The cut section was also pale and its lobular structure was obscured. The hepatic blood vessels appeared unusually crowded together, suggesting over-all structural collapse. The spleen was somewhat large (250 gm.), and its cut section was very soft. The Malpighian bodies

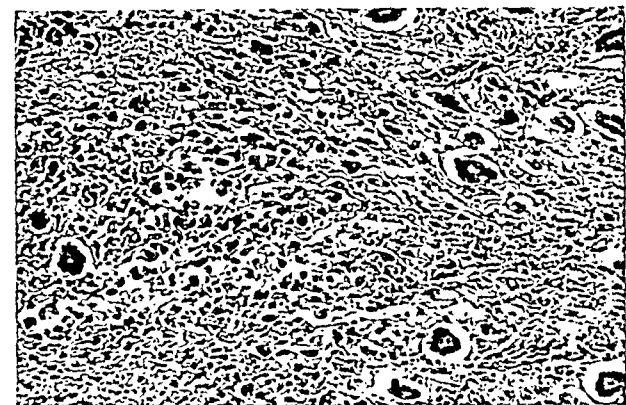


Fig. 1 (Case 1).—High-power view of the liver. Note the variation in the degree of liver necrosis and bile duct proliferation from field to field.

were quite prominent. The stomach, jejunum, and ileum contained changed blood in the lumina, and scattered submucosal hemorrhages were noted throughout the gastrointestinal tract. Grossly, the remainder of the abdominal viscera appeared normal. No thrombi were observed in the femoral veins. The dura beneath the skull defect was thickened, with a suggestion of gliosis of the underlying cortex.

On microscopic examination, the liver showed widespread necrosis with collapse of its architecture (Fig. 1 and 2). Scattered small islands of living liver cells were present in all sections. There was considerable bile duct proliferation, and an azocarmine stain did not reveal the presence of significant connective tissue. There was some hemorrhage into the collapsed framework.

As expected from the gross observation, there was a confluent lobular pneumonia of the right lung resulting from aspiration of gastric contents. The dura mater beneath the cranial defect was thickened and scarred and showed a foreign body reaction. The piaarachnoid was scarred, and the underlying right cerebral cortex showed focal gliosis with some perivascular hemorrhages.

CASE 2.—P. W., a 15-year-old white girl, was admitted on Aug. 26, 1950, to the Lutheran Hospital of Maryland. She had anorexia, nausea, and vomiting of 10 days' duration, jaundice of 7 days' duration, and apathy and confusion of several hours' duration. For the past two years the patient had been treated for idiopathic grand mal epilepsy with phenobarbital and diphenylhydantoin sodium. In June, 1950, phethenylate sodium was grad-

ually substituted for the diphenylhydantoin, so that by the following month she was receiving 0.13 gm. of phethenylate sodium four times daily with the phenobarbital.

Approximately 12 days prior to admission to the hospital she began to complain of anorexia, nausea, and vomiting. Jaundice was present the following day. No elevation of temperature was noted. She became acutely ill 10 days later and was admitted to the hospital in a semistuporous state. Physical examination revealed normal temperature, pulse, and respiratory rate. The

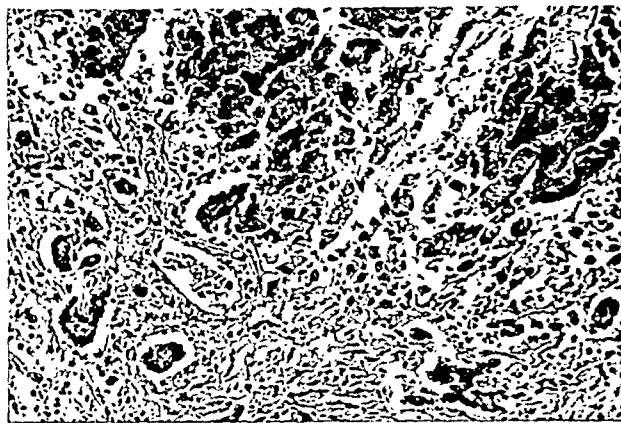


Fig. 2 (Case 1).—Another high-power view of the liver.

blood pressure was 155/95 in both arms. She was an uncooperative, confused, restless, and apathetic white girl, with a moderate degree of jaundice of the skin and scleras. The liver was tender and slightly enlarged, the lower border being palpable 2 cm. below the right costal margin.

Urinalysis revealed a trace of albumin and sugar, with 5 to 10 leukocytes per high-power field; the urine contained bile. The blood contained 12,800 leukocytes per cubic millimeter, with a normal differential count. An electroencephalogram showed an abnormal wave pattern compatible with grand mal epilepsy.

The patient's condition progressed rapidly, with stupor developing shortly after admission to the hospital. The next day she became comatose and began having very frequent short convulsions. Respiration soon became labored, and she developed slight

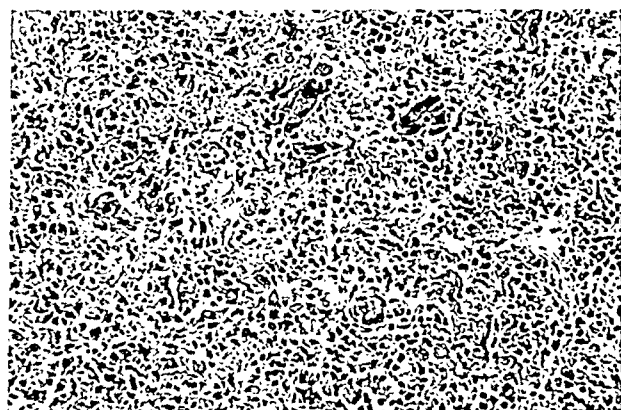


Fig. 3 (Case 2).—High-power view of the liver. All areas were similar to the one shown in the photomicrograph.

cyanosis of the nail beds. The convulsions ceased several hours later and respiration improved, but a pronounced elevation in temperature was noted at this time. Symptomatic treatment had

1. Peterman, M. G.: *Epilepsy in Childhood: Newer Methods of Diagnosis and Treatment*, J. A. M. A. 138:1012 (Dec. 4) 1948.

2. Carter, S., and Merritt, H. H.: *Medical Therapy of Epilepsy*, Journal Lancet 70:103, 1950.

3. Roach, C. E.: personal communication to the authors. Forster, F. M.: *Medical Therapy of Epilepsy*, Neurology 1:153, 1951.

been instituted immediately after admission, but the patient did not respond. Death occurred on Aug. 28, 1950, about 30 hours after admission. The clinical impression was that the patient had acute yellow atrophy of the liver secondary to phethenylate sodium therapy, or acute fulminating infectious hepatitis.

At autopsy (performed by Dr. James L. Gray) the body was 171 cm. in length and weighed about 53.5 kg. There was marked icterus of the skin and scleras. No edema was observed. When the body cavities were opened, no free fluid was noted. The liver weighed approximately 900 gm. and appeared soft. Its surface was smooth and dull yellowish-red in color. On section, its cut surface was yellowish-brown, with pinpoint red areas scattered throughout. The architecture was obscured. The spleen weighed 150 gm. and the heart 240 gm., but no significant gross lesions were noted in these organs. The lungs contained a small amount of fluid. On gross examination of the remainder of the viscera all the organs appeared to be normal, although there were signs of icterus.

Microscopically, few living liver cells could be found. There was hemorrhage into the collapsed framework. Numerous round cells and a moderate number of polymorphonuclear neutrophils were scattered diffusely through the sections. Minimal bile duct proliferation was present. Distributed throughout the collapsed tissue were phagocytic cells filled with finely divided brown pigment (Fig. 3). The lungs showed aspiration of gastric contents with edema, intra-alveolar hemorrhage, and a purulent exudate in the bronchi and bronchioles. Other sections of lung showed widely dilated cell-free alveoli. The kidneys and other viscera showed no pertinent microscopic lesions.

COMMENT

Phethenylate sodium has been shown to be an effective anticonvulsant in the treatment of epilepsy. There is, however, some disagreement as to its value in treatment of petit mal. In our experience the drug has proved more effective in the control of grand mal seizures. For the most part toxic manifestations have been mild. We have seen three patients with jaundice. In one of these cases jaundice appeared some three to four weeks after administration of the drug was started, but gradually disappeared over a period of three weeks following discontinuance of the drug. In the two cases reported here the jaundice did not appear until after the patients had taken phethenylate for approximately 6 and 24 months, respectively. Both patients died of acute hepatic insufficiency resulting from massive necrosis of the liver. Unfortunately this type of liver change occurs in cases of liver damage due to known noxious chemical agents and in cases of virus hepatitis. In neither case was there any known exposure to the virus of infectious hepatitis or a history of injections that might have been the means of infection with homologous serum jaundice. Therefore, while the virus of homologous serum jaundice cannot be conclusively eliminated as the etiological factor, the phethenylate sodium that both patients had received for treatment of epilepsy remains as a suspicious common factor in these two cases.

SUMMARY

A brief statement regarding our experience in the use of phethenylate ("thiantoin") sodium is presented. The clinical and pathological findings in two patients who died of acute hepatic insufficiency while taking the drug are given in detail.

115 E. Eager St. (Dr. Livingston).

FALSE POSITIVE REACTION TO THE PIPEROXAN HYDROCHLORIDE TEST FOR PHEOCHROMOCYTOMA

Alfred Soffer, M.D., Rochester, N. Y.

The classical clinical picture of intermittent episodes of hypertension produced by pheochromocytoma is well documented.¹ It is now established that these tumors are more often associated with sustained hypertension and that this clinical state may simulate that of essential or malignant hypertension.² In the latter cases piperoxan (benodaine³) hydrochloride as utilized in the test introduced by Goldenberg, Snyder, and Aranow in 1947, has proved to be of continuous diagnostic value.³ Goldenberg and Aranow stated in 1950 that in the several thousand tests performed in this country and in Great Britain no proved false positive results have been reported.⁴ They question the diagnosis of renal hypertension in a case presented by Taliaferro, Adams, and Haag.⁵ Palmer and Loofbourow have stated, "We know of two cases misdiagnosed, i. e., false positives."⁶ More recently (1951) Shapiro and his associates reported the specificity of this test as evidenced by their failure to elicit a typical depressor response in a control series of 30 hypertensive patients.⁷

This is a report of a false positive reaction to the piperoxan test, confirmed by autopsy.

REPORT OF A CASE

Mrs. A. B., a 57-year-old white housewife, entered the outpatient department of the Genesee Hospital on March 25, 1949, with the chief complaint of weakness and dizziness. She stated that she had been well and working until May, 1948, at which time she suffered sudden numbness of the left arm and the left leg. There was no paralysis, and after two months of bed rest

From the Heart Station and Medical Clinics of the Genesee Hospital. Dr. Jacob D. Goldstein, Chief of Laboratories, Genesee Hospital, assisted in the preparation of this manuscript and evaluated the data used. Dr. Henry Aranow, Department of Medicine, College of Physicians and Surgeons, Columbia University and Presbyterian Hospital, New York, assisted in the analysis of this report. Miss Julia Putnam gave technical assistance.

1. (a) Howard, J. E., and Barker, W. H.: Paroxysmal Hypertension and Other Clinical Manifestations Associated with Benign Chromaffin Cell Tumors (Pheochromocytomata), *Bull. Johns Hopkins Hosp.* **61**: 371, 1937. (b) Kvale, W. F.; Roth, G. M.; Clagett, O. T., and Dockerty, M. B.: Headache and Paroxysmal Hypertension: Observations Before and After the Surgical Removal of a Pheochromocytoma, *S. Clin. North America* **24**: 922, 1944.

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3. (a) Goldenberg, M.; Snyder, C. H., and Aranow, H., Jr.: A New Test for Hypertension due to Circulating Epinephrine, *J. A. M. A.* **135**: 971 (Dec. 13) 1947. (b) Cahill, G. F.: Pheochromocytomas, *ibid.* **138**: 180 (Sept. 18) 1948.

4. Goldenberg, M., and Aranow, H., Jr.: Diagnosis of Pheochromocytoma by the Adrenergic Blocking Action of Benzodioxan, *J. A. M. A.* **143**: 1139 (July 29) 1950.

5. Taliaferro, I.; Adams, R. A., and Hagg, H. B.: Benzodioxan Test: A Fall in Blood Pressure Following Its Use in a Case of Renal Hypertension, *J. A. M. A.* **140**: 1271 (Aug. 20) 1949.

6. Palmer, R. S., and Loofbourow, D., in Conn, H. F., and others: *Current Therapy 1950: Latest Approved Methods of Treatment for the Practicing Physician*, Philadelphia, W. B. Saunders Company, 1950.

7. Shapiro, A. P.; Baker, H. M.; Hoffman, M. S., and Ferris, E. B.: Pharmacologic and Physiologic Studies of a Case of Pheochromocytoma, *Am. J. Med.* **10**: 115, 1951.

there was some return of strength. In the following months she experienced occasional headaches, lightheadedness with change in position, and almost constant fatigue.

The past history included asthmatic attacks relieved by aminophylline and epinephrine and an episode of hives. Neither of these had occurred recently. More recently the patient had noted "spots before the eyes" and increased difficulty in hearing. The family history was not contributory.

The physical examination revealed a somewhat obese but well-developed woman, who seemed to be somewhat confused. Answers to question were delayed, perhaps because of difficulty in hearing.

The lungs were clear to percussion and auscultation, but percussion of the heart revealed the apex to be nearly at the left anterior axillary line. A soft apical systolic murmur was present. Results of the neurological examination were not remarkable. The blood pressure was 200/130. The patient stated that her blood pressure in the previous year had ranged from extremes of 150/110 to 240/140. The patient's weight at this time was 162½ lb. (73.8 kg.).

The laboratory studies revealed normal hemoglobin, white blood cell, and red blood cell values. The urine contained albumin (2+); this was found on repeated analyses during the following year. The blood urea nitrogen was 17 mg., and the blood sugar 92 mg. per 100 ml. The Wassermann reaction was negative. The chest roentgenogram revealed cardiac enlargement, the transverse diameter of the heart measuring 15 cm. The contour was of an "aortic" type and the descending aorta was wide-swinging. The electrocardiogram indicated left ventricular hypertrophy and strain. The ballistocardiogram showed a markedly abnormal pattern; the irregular, indefinite complexes were of low amplitude. Breath holding revealed more definite complexes.

The patient was seen as an outpatient at least every month during the next year and a half. During this time the blood pressure ranged between 280/160 and 190/115. With encouragement the patient was able to lose 33 lb. (15 kg.). Veratrum viride medication was tried for a period of two months, and the dosage was increased gradually to 60 Craw units divided into two daily doses. This was stopped on Sept. 30, 1949, because of side-effects and because no lasting objective or subjective improvement was achieved. A urea clearance test showed 35% of maximum clearance at the end of two hours; the blood urea nitrogen at this time was 28 mg. per 100 ml. The pulse rate during this period of observation ranged between 65 and 78. Various observers noted hemorrhages and exudates in the retinal fundi, but these were described as old. Traces of sugar in the urine were found occasionally. Fatigue, dizziness, and weakness persisted and grew worse.

On Sept. 13, 1950, the patient was admitted briefly to the hospital because of an episode of lethargy and drowsiness associated with headache and weakness. The clinical diagnosis on this occasion, as on the next admission, was hypertensive arteriosclerotic encephalopathy and hypertensive cardiovascular disease with probable renal involvement. The blood pressure was 290/145, the fasting blood sugar level was 102 mg. per 100 ml., and the nonprotein nitrogen level was 66 mg. per 100 ml. The patient improved somewhat, and it was decided to send her to a nursing home.

At the time of the final hospital admission on Nov. 17, 1950, the patient was vomiting and somewhat unaware of her surroundings. At this time the blood urea nitrogen level was 56 mg., and the serum uric acid 10.5 mg. per 100 ml. The serum carbon dioxide combining power, sodium, chloride, and creatinine determinations were within normal limits. On November 19 the patient fell out of bed but suffered no damage other than a bruised hip. At the time of this episode the blood pressure was recorded as 300/200. By November 24 the blood urea nitrogen had risen to 82 mg. per 100 ml.; clinically the patient was considered to be confused. Barbiturates were not administered during the final hospital stay; 30 cc. of milk of magnesia November 26 was the only medication given. On November 27 the patient became stuporous. Funduscopic examination revealed marked arteriolar constriction and blurring of both disk margins. On this day a lumbar puncture was done and an opening pressure of 300 mm. was recorded. Clear spinal fluid was collected; it contained no cells, but the spinal fluid protein

was 90 mg. per 100 ml. On the same afternoon a piperoxan test was performed. Because of the stuporous condition, an intravenous infusion to serve as an introductory venous puncture was, of course, not needed. Preliminary determinations of the blood pressure were recorded every minute for 15 minutes; 16 mg. of piperoxan hydrochloride was injected intravenously at 3:45 p. m. during a one to two-minute interval. The results are recorded in Figure 1. The nurses' notes include a blood pressure determination of 220/150 made an hour later. Approximately 6 to 10 hours later the blood pressure was unobtainable and the patient was semicomatose; left facial weakness was present, and all the extremities were flaccid. The pulse was rapid but readily palpable. Cheyne-Stokes respirations began that afternoon, diaphoresis was marked, and frequent suction was required to keep the oropharynx free of thick and abundant mucus. The urinary output on November 26 was 650 cc., on November 27 675 cc., and on November 28 only 375 cc. Subcutaneous and intravenous infusions of 5% dextrose in water were used to maintain an adequate fluid intake. An electrocardiogram taken on the afternoon of November 29 indicated increasing myocardial ischemia and evidence of epicardial injury in the high lateral leads (Fig. 2). The patient died a few hours later, at 7:30 p. m.

NECROPSY REPORT

Gross Findings.—Heart: The heart weighed 550 gm. The myocardium was brownish red and firm. Several small areas of scarring were present, but there was no evidence of confluent infarction. The chambers were all increased in size, especially the left

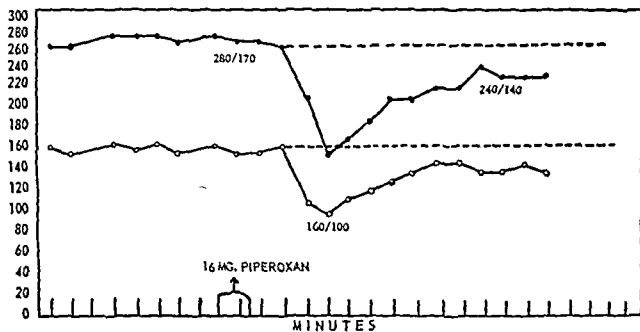


Fig. 1.—Blood pressure changes following the administration of 0.16 mg. of piperoxan hydrochloride.

auricle and left ventricle. The left ventricular wall was 2 cm. thick and the right ventricular wall 0.6 cm. The coronary vessels were of fairly good caliber, but exploration showed scattered, small yellowish plaques on the endothelial lining.

Adrenals: The adrenals were normal in size and rather soft. On cut section the three zones were readily demonstrable in their normal relationship.

Kidneys: The left kidney weighed 80 gm., the right 70 gm. They were purplish gray, but after the capsules were stripped the surfaces were seen to be reddish brown and rough. The cortex of each kidney was yellow and 0.3 cm. thick; the usual striations were not seen. Glomeruli could not be identified. The pyramids were reduced in size. The calyces and pelves were approximately normal in size, and the mucosa of the pelvis was whitish and smooth.

Lungs: On cut section the parenchyma of the upper portions of both lungs were grayish pink and had a fluffy consistency. No increase in wetness was noted. The lower lobes were similar except for scattered portions, which were very red and slightly wet.

Brain: In the lateral and basilar area of the right temporal lobe at the level of the optic chiasm there was a spherical 6 mm. reddish black area of recent hemorrhage. In the putamen and internal capsule on the right, just posterior to the area described above, there were a few streaks of depressed, translucent, old encephalomalacia.

Histological Studies.—Heart: Edematous, hypertrophied cardiac muscle in branching bundles was noted. Polynuclear leukocytes were present between some of the muscle bundles. Scattered small areas of scarring were present in the myocardium. The endocardium was smooth.

Adrenals: Sections showed a normal capsule, epithelial cells arranged in three zones, and, in the medulla, some chromaffin cells containing minute granules. In some areas partial autolysis of the epithelial cells was noted. Marked sclerosis of the capsular arterioles was seen.

Kidneys: Sections showed pronounced sclerosis of the small arteries and arterioles (Fig. 3). There was fibrosis of many of the glomeruli, and numerous segments of tubular epithelium showed atrophy. Moderate numbers of lymphocytes infiltrated the atrophied parenchyma. The remaining tubules were dilated and generally filled with pink granular casts. A few hemorrhages

were seen in the pyramidal tissue. Moderate numbers of lymphocytes were seen beneath the calyces.

Lungs: Sections showed smooth pleura. Areas of emphysema and atelectasis were noted. The alveolar walls were edematous in varying degrees and the alveolar capillaries congested. There were scattered areas in which there were decided edema and

congestion of the alveolar walls and many polymorphonuclear cells, round cells, fibrin, and red blood cells in the alveoli. Some alveoli contained fat vacuoles. Many polymorphonuclear cells and fibrin were seen in the bronchioles.

Brain: The sections showed some focal hemorrhages and areas in which there was slight necrosis of tissue, fibroblasts, and macrophages.

Final Pathological Diagnoses.—(1) Chronic pyelonephritis and marked arteriolar nephrosclerosis; (2) generalized arteriosclerosis and arteriolar sclerosis; (3) cardiac hypertrophy and dilatation; (4) bronchopneumonia and lipoid pneumonia; (5) cerebral edema; (6) focal cerebral hemorrhages and old encephalomalacia.

COMMENT

The magnitude of the immediate blood pressure drop following the administration of piperoxan (benodaine®) hydrochloride and the slope of the recovery curve characterizes this as a definitely positive reaction. The dosage

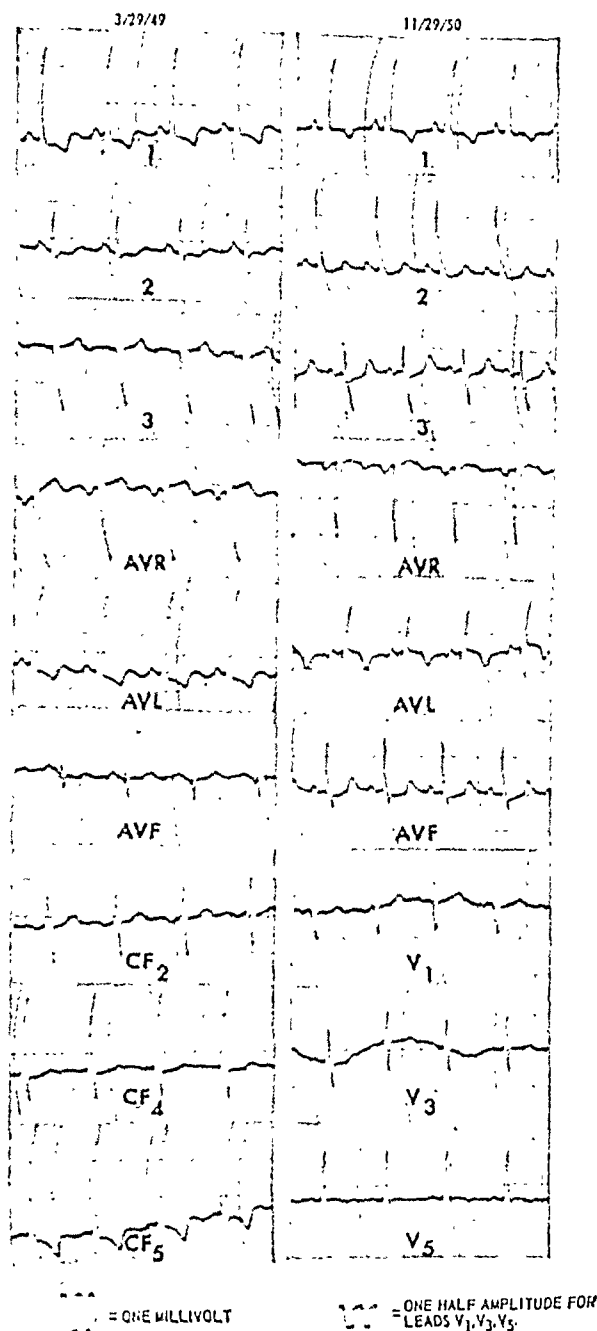


Fig. 2.—Comparison of electrocardiograms. The tracing taken shortly before the patient died (Nov. 29, 1950) shows evidence in the high lateral leads of acute epicardial injury when contrasted with an earlier electrocardiogram, taken on March 29, 1949.

were present in the pyramidal tissue. Moderate numbers of lymphocytes were seen beneath the calyces.

Lungs: Sections showed smooth pleura. Areas of emphysema and atelectasis were noted. The alveolar walls were edematous in varying degrees and the alveolar capillaries congested. There were scattered areas in which there were decided edema and



Fig. 3.—Photomicrograph of kidney, demonstrating arterial and arteriolar nephrosclerosis.

used has been well standardized, i. e., approximately 0.25 mg. per kilogram of body weight or 10 mg. per square meter of body surface. Sedatives were not administered to this patient, and a barbiturate-piperoxan interreaction (which may be demonstrated experimentally^{3a}) could not therefore have been present. The autopsy revealed the absence of a chromaffinoma of the adrenal glands or in the other sites⁸ in which such tumors may occur. (Theoretically a tiny portion of actively secreting chromaffinoma tissue present in an aberrant location could be missed by the most careful pathologist.⁹) The extent of the renal involvement indicates that it is unlikely that the markedly shrunken kidneys were secondary to hypertension produced by a pheochromocytoma.^{1a} In view of these considerations this piperoxan test must be said to have produced a false positive result. The unusual circumstances under which this test was performed should be noted, including the semistuporous condition of the patient and the uremic blood urea nitro-

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gen level. (It may be added that the value of performing this diagnostic procedure on a patient so critically ill must be questioned.)

An observer cannot with certainty attach a cause-and-effect relationship between the transient blood pressure response to piperoxan and the appearance of shock a few hours later, which persisted until death. The appearance at any time of an acute cerebral or cardiac episode or a rapidly progressive downhill course was entirely consistent with the patient's critical condition. However, the dramatic change in the patient's clinical status following the temporary but pronounced blood pressure drop a few hours earlier should warrant consideration. Investigators have noted the drastic effects that sudden blood pressure changes can produce in patients or experimental subjects with lowered circulatory reserves.¹⁰ Guarneri and Evans noted that the transient blood pressure drop produced by the administration of methacholine (mecholyt®) to hypertensive patients precipitated a convulsion in one case and substernal pain in another.¹¹ The blood pressure level may be "normal," but in a hypertensive patient such a blood pressure level may indicate the presence of shock. The dangers of a sudden drop to such blood pressure levels in the older age groups are emphasized by Corday and collaborators.¹² In opposition to the view that the patient's terminal relapse may have been related to the piperoxan test is the pertinent fact that the blood pressure returned almost to the resting level after a few minutes and remained so for a latent period of a few hours before terminal shock appeared. Wilkins and collaborators state that 8% of the patients in a series of 75 hypertensive patients responded to the piperoxan test with alarmingly severe reactions, primarily pressor in nature,¹³ but Goldenberg and Aranow report in the same month (July, 1950) that in a large number of piperoxan tests (several thousand) there have been few toxic effects and no instances of persistent damage.⁴

CONCLUSION

A case of a false positive reaction to the piperoxan test for pheochromocytoma is described, and the autopsy findings are reported. The effects of sudden blood pressure changes in patients with lowered circulatory reserves are reviewed, and the possible relationship of these phenomena to this case is discussed. It is concluded that it does not seem probable that the transient blood pressure fall observed was directly related to the outcome.

224 Alexander St.

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SPOROTRICHOSIS

REPORT OF TWO CASES FROM UTAH

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and

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Sporotrichosis has been regarded as a rare disease. In recent years, however, cases have been reported with increasing frequency, probably because of an increased alertness on the part of the medical profession. Most cases in this country have been reported from the Mississippi valley; none have been reported from Utah or from this part of the country so far as we have been able to ascertain. We believe that these cases are worthy of reporting because of this fact, and also because in one of our cases a trial with some of the newer antibiotics was carried out without apparent effect. These patients lived in the same county, within two or three miles of each other.

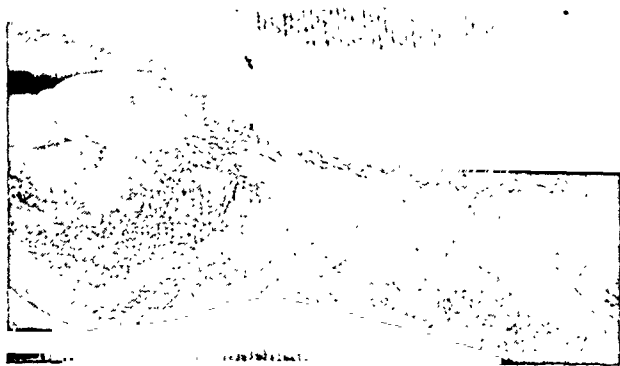


Fig. 1 (Case 1).—Nodules on the dorsum of the left hand and extending up the forearm.

REPORT OF CASES

CASE 1.—A man aged 55, a miner who worked underground in a silver, lead, and zinc mine in Salt Lake County scratched his hand on Sept. 20, 1949, while working in the mine. It was treated by application of antiseptics. Within a few days it became infected, and for nine days it was treated with hot applications. About a month later the infection seemed to spread upward from the forearm and arm, producing multiple subcutaneous nodules which were slightly painful, some of these broke down spontaneously and drained. He was treated by his local physician, who incised several of the nodules and gave him penicillin periodically during the course of the disease.

He was first seen by one of us on November 7 and was sent to the hospital immediately. Smears, cultures, and two biopsy specimens were taken within a few hours of admission. One of the specimens was removed from the edge of an ulcer on the hand and the other from a nodule just above the elbow. On examination at the hospital an ulcerated lesion was found on the dorsal of the phalanx of the middle finger of the left hand. It was about 1 cm. in diameter with raised edges and a rather dirty, purulent discharge. There was moderate tenderness. On the dorsum of the hand were many small nodules in close apposition; extending up the forearm and for several inches above the elbow were numerous hard, red, small nodules, about 1 cm. in diameter. There was no enlargement of the axillary lymph nodes. Temperature and pulse were normal. Laboratory examination on admission showed the hematocrit reading to be 46, the white blood cell count 8,800 per cubic millimeter, and the hemoglobin value 16 gm. per 100 cc. The differential cell count showed 71% segmented forms, 19% lymphocytes, 2% monocytes, 5% stab forms, and 3% eosinophils. Urinalysis showed a specific gravity of 1.023 and no albumen or sugar; microscopic examination

showed 1 to 4 pus cells per high powered field and a few epithelial cells. A smear from the ulcer of the hand contained a few pus cells. A culture revealed typical *Sporotrichum*, which will be described later. Other blood studies included blood cultures and agglutination tests, including the Widal test, tests for paratyphoid A, paratyphoid B, brucellosis, tularemia, and *Proteus vulgaris* OX19, all of which gave negative results.

The pathological report was made by Dr. Crichton McNeill. The excised nodule from the arm measured 1.8 by 1.5 cm., the exterior showed normal fatty tissue with gray areas interspersed. Cut section showed a mottled yellow-gray central portion, with small hemorrhagic areas. The specimen from the hand lesion was a small, irregular, gray nodule of fixed tissue measuring about 8 mm. in diameter. Microscopically, the section of the ulcer of the hand showed a moderate epitheliomatous hyperplasia and granulation reaction. The main cellular infiltration appeared to be plasma cells and lymphocytes in the area of the ulcer and beneath the epithelium. Deep in this portion there was one site which was interesting, in that slender gram-positive bodies were seen under oil immersion. These bodies also had small spores attached to them or nearby. These small round spores were distinctive in that they took a deep blue color and showed no evidence of nuclei and were therefore not lymphocytes. This appeared to be conclusive evidence that there was a fungus growing in the deeper aspects of the granulation tissue. The section taken from the forearm showed a granulomatous reaction without evidence of spore-forming or mycelial tissue. The main cellular reaction again was lymphoid elements and plasma cells. There was an increase in fibrous tissue, and reticulum cells appeared to be present. No well-developed giant cells, were present. The pathologic diagnosis was granulation tissue due to a fungus, later identified as *Sporotrichum*.

The patient was treated with bed rest, elevation, and hot packs. He had received considerable penicillin periodically in previous weeks. Aureomycin hydrochloride therapy was started on the day after admission; it was given in doses of 250 mg. three times a day beginning on November 13. On November 19 aureomycin therapy was stopped, and chloramphenicol (chloromycetin[†]), 250 mg. three times a day, was administered until November 25, when treatment with potassium iodide in usual dosage was begun. During the administration of aureomycin and chloramphenicol, little or no improvement could be noted except some clearing up of the dirty ulceration of the hand, which was probably due to elevation and hot packs. After potassium iodide therapy was started, improvement was prompt.

The patient was discharged from the hospital on November 26 and was treated as an office patient until his final discharge, on Jan. 3, 1950, when the lesions were completely healed. There has been no evidence of recurrence or relapse.



Fig. 2 (Case 2).—Ulcerated lesion on the dorsum of the left arm near elbow. Half way between wrist and elbow is another open and ulcerated area.

CASE 2.—A 15-year-old boy was first seen Nov. 28, 1949. Two months earlier he had noted sores on his left arm. After he had been playing football a sore similar to a mosquito bite appeared on the dorsal aspect of his left hand. He scratched it, and it subsequently developed into an open running sore. This sore then began spreading up the inner aspect of his arm. Stiffness

developed in his arm, and he noted increasing fatigue. He gave no history of chills or fever. He was given penicillin and a sulfonamide for three weeks without improvement. X-rays of the arm were reported as normal. There was no history of having been bitten by a deer fly or of having been around rabbits.

On physical examination the important clinical findings were limited to his left hand and arm. On the dorsal aspect of the left arm, in the region of the wrist, there was a punched-out ulceration measuring approximately 1 cm. in diameter. Around

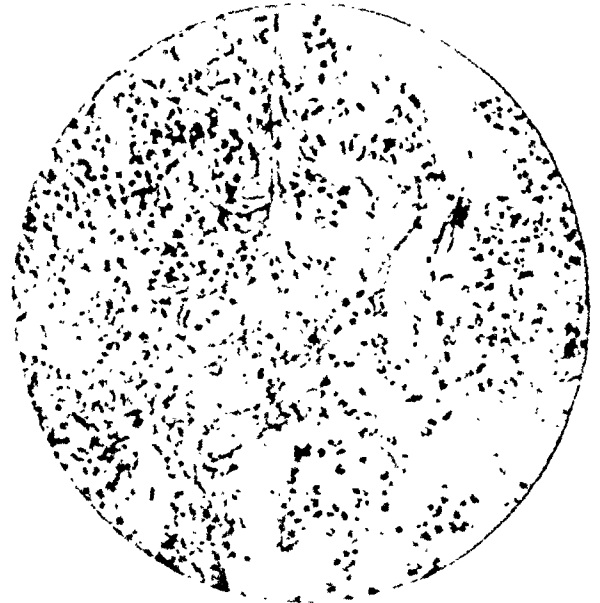


Fig. 3.—*Sporotrichum schencki* as seen in biopsy section.

this was an area of considerable redness and induration, but there was practically no tenderness. A yellowish fluid was draining from the ulcerated area. Along the ulnar side of the arm, half-way between the wrist and the elbow, was another open and ulcerated area; and in the region of the elbow on the inner aspect and all the way up to the axilla were numerous shot-like lymph nodes. One node near the elbow was definitely fluctuant. The temperature was normal, the pulse rate 84, and weight 47.6 kg. (105 lb.).

Urinalysis showed a specific gravity of 1.028, acid reaction, no albumin, no sugar, and no abnormal microscopic findings. The hemoglobin value was 92%, or 14.3 gm.; the red blood cell count was 4,071,000; the white blood cell count was 8,800; sedimentation rate (Westergren) was 30 mm. in one hour. Agglutination tests were made for tularemia and brucellosis, and all were reported as negative.

Pus from the lymph node near the elbow was then aspirated, and cultures were sent to the University of Utah Bacteriology Laboratory, where a pure culture of *Sporotrichum schencki* was grown. The patient was then given 15 drops of saturated potassium iodide solution three times a day, and the dose was increased to the limit of tolerance. Under this treatment the ulcers promptly began to heal, and he made a complete recovery in about six weeks.

COMMENT

Sporotrichosis was first described by Link in 1809. Schenck, in 1898, was the first to isolate the fungus and to prove its etiologic relationship. Much of our present knowledge of the disease is due to the investigations of De Beurmann and Gougerot, who in 1912 published a monograph in two volumes on the disease. It is generally accepted that there are at least two varieties of organisms, the *S. schencki* and *S. beurmanni*. The former is believed to be the usual variety in the United States, and the latter is said to occur most commonly in France. Radiate formation, sometimes called asteroid formation, has also been described and may represent an entirely different species (*S. asteroides*).¹ These star-shaped

¹ Moore, M., and Ackerman, L. V. Sporotrichosis with Radiate Formation in Tissue: Report of Case. Arch. Dermat. & Syph. 53:253, 1945.

bodies are found extracellularly in pus, and most of the reported cases of this type are from South America.

Sporotrichum has been found in all parts of the world, usually as a saprophyte on flowers, grains, grasses, bark, thorns, and vegetables, and also on fleas, ants, and various forms of insects. It has been found in apparently normal throats and normal intestinal tracts. It seems probable that the organism invades the human via minor wounds of the skin, especially of the fingers, hands, or feet, since these sites are involved in most clinical cases.² Two cases have been reported of investigators contracting sporotrichosis while working with cultures of the organism. In other cases the disease has been contracted from handling infected dressings. Most clinical cases have occurred in farmers or florists.³

The organism is usually of low virulence. It is aerobic and grows well on ordinary culture media such as Sabouraud's medium at room temperature. The colony becomes apparent in a few days as a white growth with radiating lines at right angles to the margin. Later the growth darkens to gray or almost black. Microscopically, a great abundance of mycelia, with short branches extending outward and supporting microconidia, are seen. Although it is usually impossible to find the organism on biopsy specimens, this was accomplished in one of our cases.

The disease has been produced experimentally in horses, cats, mice, monkeys, guinea pigs, and rats. Rats are particularly useful for inoculations in establishing the diagnosis. Two forms of the disease have been reported—the lymphatic and the systemic or disseminated form.⁴ In this country the lymphatic is the usual form, while in France the systemic is apparently the more common. Both of our cases fall into the lymphatic group. In this form the initial lesion is a chancre-like ulcer usually



Fig. 4.—Appearance of *Sporotrichum schencki* growth on culture plate.

on a finger, hand, or foot. In about three weeks to three months a chain of nodules appear in ascending fashion along the course of the lymphatics. These are red, firm, discrete, painless lesions which may ulcerate and become infected. When ulceration is present the floor of the ulcer is found to be granular. It bleeds easily and tends to become covered by a crust; sinuses may form around it. The lesion is essentially a granuloma with three zones. In the peripheral zone there is marked connective tissue

reaction with vasodilation, plasma cells, and lymphocytes. In the middle zone are numerous epithelioid cells and abundant giant cells grouped more or less like tubercles. In the center are polymorphonuclear leucocytes, eosinophils, macrophages, etc., with microabscesses.

There are frequently no systemic symptoms, but in the very acute cases fever, chills, and signs of septicemia may

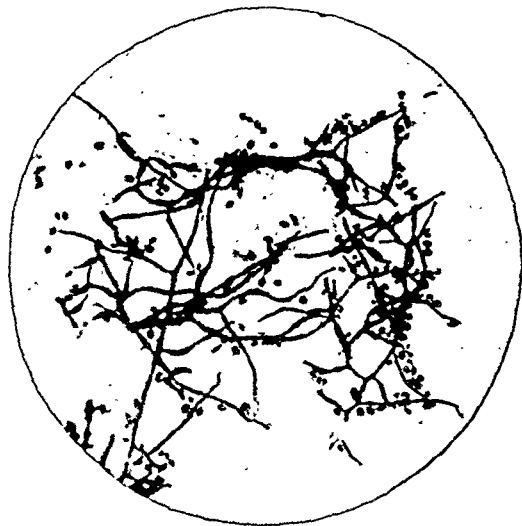


Fig. 5.—Microscopic appearance of organism.

develop. In long-continued cases, anemia, loss of weight and strength, and general debility may develop. Lungs, bones, muscles, glands, joints, viscera, mouth, pharynx, and even the central nervous system may be involved.⁵ Patients who have had the disease in the pharynx may retain the organism after recovery and act as carriers. Treatment consists of the administration of a saturated potassium iodide solution. This is given by mouth, starting with 10 minims (0.6 cc.) three times a day and increasing 1 minim (0.06 cc.) three times a day to tolerance. Iodine may also be applied locally. X-ray therapy has been used with good results in a few cases. There seems to be little or no tendency for spontaneous involution to occur. The disease may persist for months or years if untreated.

508 E. South Temple (Dr. Castleton).

2. (a) Holland, M. H., and Mauriello, D. A.: Sporotrichosis, *J. M. Soc. New Jersey* 46: 419 (Sept.) 1949. (b) Madden, J. F.: Sporotrichosis in Minnesota, *Minnesota Med.* 30: 854, 1947.

3. Gelber, A.: Sporotrichosis: Report of a Case of Its Occurrence in California, *Arch. Dermat. & Syph.* 54: 208, 1947.

4. Cawley, E. P.: Sporotrichosis, A Protean Disease: With Report of a Disseminated Subcutaneous Gummatous Case of the Disease, *Ann. Int. Med.* 30: 1287, 1949.

5. Banks, H. S.: Sporotrichosis Resembling Diphtheria: Report of Unusual Case, *Lancet* 2: 270, 1946.

Abdominal Pain.—Referred abdominal pain attending the diaphragmatic inflammation of pneumonia may usually be so diagnosed with the demonstration that the peritoneum is not tender on percussion, therefore, not inflamed, and therefore not the primary source of the abdominal pain. A case of abdominal pain unaccompanied by tenderness anywhere on moderate to heavy percussion may be confidently held for further observation without fear that an acute surgical emergency is being overlooked.—Emile Holman, M.D., *The Art of Abdominal Percussion in the Presence of Inflammation, Surgery, Gynecology and Obstetrics*, December, 1951.

ACUTE ULCERATIVE ENTERITIS DUE TO POLYARTERITIS

A DIAGNOSTIC DILEMMA

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and

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Polyarteritis was described in 1866 by Kussmaul and Maier as periarteritis nodosa. Polyarteritis is a more exact name, since all coats of the vessel are involved and since nodules may not always be present. It is a widespread disease of arteries, and less commonly of veins, which may affect any organ or tissue of the body. This is a report of a case of polyarteritis with acute ulcerative enteritis. The diagnosis was not made until tissues secured at autopsy were examined. A review of the literature to November, 1950, confirmed our diagnosis. Polyarteritis is a rare causative agent in gastrointestinal ulceration.

REPORT OF CASE

History.—S. L., a 52-year-old Negro housewife, was admitted to the hospital complaining of epigastric pain of two months' duration. She was awakened by severe epigastric pain which radiated along the margins of the costal cage. Except for varying intensity, it never completely disappeared. Episodes of nausea and vomiting were frequent. There was no diarrhea or melena. Anorexia and a loss of 41 lb. (18.6 kg.) occurred in this two-month period. She had been treated in 1914 for gonorrhea and in 1919 for syphilis. There was no history of rheumatic fever, diabetes mellitus, malaria, tuberculosis, or cancer.

Physical Examination.—The patient was a poorly nourished, middle-aged Negro woman, who appeared chronically ill and older than her stated age. The skin was hot and dry, and the mucous membranes were pale. There was grade III hypertensive retinopathy. Minimal cervical adenopathy was present, and her breasts were atrophic. The heart was normal, the pulse rate 100, and the blood pressure 190/120. Respirations were 24 per minute. Lung fields were clear to percussion and auscultation. Epigastric tenderness was elicited, and the liver edge was palpable. The genitals and extremities were normal. The temperature during hospitalization ranged from 99 to 102.4 F.

Laboratory Data.—Examination of the blood on admission showed a hemoglobin content of 10.6 gm., 4,100,000 erythrocytes, and 12,800 leucocytes, with 80% neutrophils, 17% lymphocytes, and 3% monocytes. Examination of the bone marrow disclosed nothing remarkable. The sedimentation rate was normal. The urine contained albumin (3+). Microscopic examination showed numerous red and white blood cells and an occasional hyaline cast. The reaction of the blood to the Wassermann and Kahn tests was negative. Tests of hepatic and renal function provided responses within normal limits. The results of serum amylase tests were less than 80 units. Special pancreatic studies revealed normal glandular function. Titration of gastric residues showed no free acid and a total acidity up to 29 units; microscopic examination showed a few red blood cells. On many occasions occult blood was demonstrated in the stool. The reaction to the tuberculin test with 0.005 mg. of purified protein derivative was positive, and the skin failed to react to blastomycin, coccidiomycin and histoplasmin antigens. There was no reaction to serologic tests for amebiasis, trichinosis, or echinococcosis. Results of cerebrospinal fluid tests were normal. Sigmoidoscopic visualization demonstrated a diffuse redness and granularity of the mucosa of the lower bowel and the presence of thickened mucus. This evidence was considered suggestive of non-specific ulcerative colitis. Roentgenographic examination included a skeletal survey, chest roentgenograms, swallowing function with upper gastrointestinal and small bowel study,

barium enemas, cholecystograms, and intravenous urograms. None of these procedures yielded a diagnostic clue. Microscopic examination of a section of an inguinal lymph node revealed hyperplasia of the reticulum cells.

Clinical Course.—In addition to the epigastric pain, the patient complained of generalized arthralgia. Abdominal tenderness increased, and distention appeared. Vomiting accentuated the dehydrated condition, and it was necessary to give fluids intravenously. The blood pressure varied from 190 to 135 systolic and from 125 to 90 diastolic, and there was a low-grade fever. Her condition became progressively worse. She died a few hours after unsuccessful attempts had been made to substantiate the presence of intestinal obstruction by roentgenography. Clinical impressions were as follows: peptic ulcer, possibly malignant; carcinomatosis, primary in the gastrointestinal tract; or abdominal Hodgkin's disease.

Necropsy Report.—The body was that of an elderly appearing, emaciated Negro woman. Abdominal distention was prodigious. On section, dilated loops of bowel bulged beneath an



Fig. 1.—Ileum with irregular, solitary, and confluent superficial mucosal ulcerations (fixed specimen).

apron of congested, thickened omentum. There were diffuse serosal petechiae. Careful search failed to disclose obstruction or perforation of the bowel. More than 500 cc. of a serosanguineous fluid was found in the peritoneal and pleural cavities. A superficial ulcer, 2 by 0.2 cm., was noted midway along the greater curvature of the stomach. The edges were slightly raised, rolled, and undermined, while the base was gray and granular. Duodenal and jejunal mucosal surfaces showed congestion. The ileum was replete with irregular superficial ulcers. Some were confluent, and as such measured up to 7 by 3.5 by 0.15 cm. (Fig. 1). A few small ulcers were found scattered throughout the colon, but none were found in the rectum. Cultures of the ulcers and the exudate in the peritoneal cavity yielded *Bacillus coli communis*, *Staphylococcus pyogenes* var. *aureus*, nonhemolytic streptococci, and diphtheroid bacilli.

Microscopic Findings.—An unexpected lesion, polyarteritis, was found to be the cause of the acute ulcerative enteritis. The small arteries and arterioles of the gastric and intestinal walls

and of the mesentery disclosed changes which could be divided into four phases (as suggested by Arkin¹): (1) degeneration, (2) acute inflammation, (3) granulation, and (4) healing. All these stages were found in this case. Initially, there was medial degeneration with nuclear and cellular fragmentation (Fig. 2). Second, acute inflammation was manifested by edema and in-



Fig. 2.—Medial degeneration (hematoxylin and eosin $\times 50$).

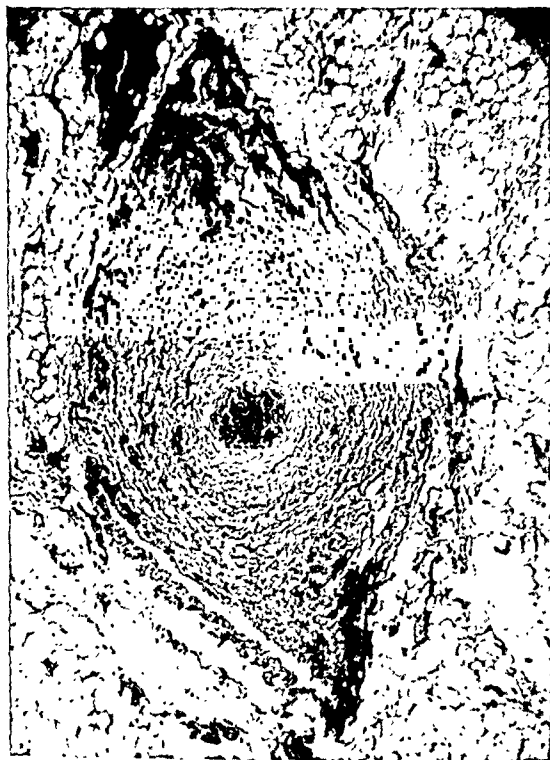


Fig. 3.—Acute inflammation and thickening of the media resulting from edema and infiltration with neutrophils, lymphocytes, and eosinophils. Note the luminal occlusion by fresh thrombus formation (hematoxylin and eosin $\times 100$).

filtration of the vascular coats with neutrophils, lymphocytes, and eosinophils. Hemorrhagic infarcts and thrombosis were observed in some sections (Fig. 3). Third, fibroblastic proliferation was noted in the zone of inflammation, with a decrease in the number of neutrophils and an increase in lymphocytes and

plasma cells—all of which coincided with Arkin's stage of granulation (Fig. 4). Fourth, lumens of the arterioles were reduced or obliterated and their walls replaced with scar tissue and periarteriolar fibrosis (Fig. 5). These lesions were interpreted as vascular changes consistent with polyarteritis. They were present to a lesser degree in the pancreas, liver, thyroid gland, and kidneys.

COMMENT

Acute ulcerative enteritis caused by polyarteritis is infrequent. Perusal of the literature fails to produce standards on which we can base the actual incidence of intestinal ulceration caused by polyarteritis. Recently, Wold and Baggenstoss,² in a report based on 30 cases of polyarteritis in which necropsy was performed, found one case with hemorrhagic ulcers and necrosis in the colon and rectosigmoid. However, they noted inflammation of the small arteries and arterioles in the jejunum in 37%, in the ileum in 27%, and in the colon in 20% of the



Fig. 4.—Granulation-tissue stage with fibroblastic proliferation and perivascular infiltration with lymphocytes and plasma cells (hematoxylin and eosin $\times 50$).

30 cases. From their study it was apparent that any portion of the gastrointestinal tract may be involved by polyarteritis. It is significant that vascular lesions of the gastrointestinal tract and the principal symptoms of abdominal pain occurred in 21 (70%) of the 30 cases.

Later in the same year, Johnson and Baggenstoss³ reported polyarteritis involving the mesenteric arteries in 3 of 60 cases of arterial occlusion. In one of these the entire jejunum and ileum were the sites of infarction, while, in the other two cases, numerous small areas of

1. Arkin, A.: A Clinical and Pathological Study of Periarteritis Nodosa, *Am. J. Path.* 6: 401 (July) 1930.

2. Wold, L. E., and Baggenstoss, A. H.: Gastrointestinal Lesions of Periarteritis Nodosa, *Proc. Staff Meet., Mayo Clin.* 24: 28 (Jan. 19) 1949.

3. Johnson, C. C., and Baggenstoss, A. H.: Mesenteric Vascular Occlusion: II. Study of 60 Cases of Occlusion of Arteries, and of 12 Cases of Occlusion of Both Arteries and Veins, *Proc. Staff Meet., Mayo Clin.* 24: 649 (Dec. 21) 1949.

the intestine showed evidence of infarction which gave the appearance of mucosal ulcers. Most recently, Sandler and associates,⁴ described a case of polyarteritis with pulmonary cavitation. They casually referred to the concomitant presence of several superficial ileal ulcerations measuring up to 4 by 1.5 cm.

The literature concerned with polyarteritis abounds with reports on the incidence of coexistent abdominal symptoms and gross vascular lesions, but only sporadic mention is made of the simultaneous presence of intestinal ulceration. Pathologically, the intestinal lesions vary from solitary, minute, isolated foci to confluent and massive ulceration. Acute involvement of the stomach or bowel wall may lead to perforation, and fatal peritonitis. The submucous and muscular coats are affected initially, but later erosion and ulceration of the overlying mucosa

carcinoma of the stomach or of the gastrointestinal tract. It is not uncommon for the patient to exhibit signs of intestinal obstruction as a terminal event. Thus, in retrospect, it is apparent that the case here presented was typical of polyarteritis.

SUMMARY

Acute ulcerative enteritis resulted from vascular thrombosis secondary to the inflammatory changes in the small arteries and arterioles. The diagnosis, which had completely baffled the clinicians, was made after microscopic examination of tissue secured at autopsy. From a study of this and other cases, it is apparent that polyarteritis is an occasional cause of intestinal ulceration.

U. S. Naval Hospital, Beaufort.

4. Sandler, B. P.; Matthews, J. H., and Bornstein, S.: Pulmonary Cavitation Due to Polyarteritis, *J. A. M. A.* 144: 754 (Oct. 28) 1950.

5. Felsen, J.: Sigmoidoscopic Diagnosis of Periarteritis Nodosa, *Ann. Int. Med.* 15: 251 (Aug.) 1945.

6. Logue, R. B., and Mullins, F.: Periarteritis Nodosa: Report of 11 Cases with Review of Recent Literature, *Ann. Int. Med.* 24: 11 (Jan.) 1946. Diaz-Rivera, R. S., and Miller, A. J.: Periarteritis Nodosa: A Clinicopathological Analysis of 7 Cases, *Ann. Int. Med.* 24: 420 (March) 1946. Miller, H. G., and Daley, R.: Clinical Aspects of Polyarteritis Nodosa, *Quart. J. Med.* 15: 255 (Oct.) 1946. Rose, M. H.; Littman, D., and Houghton, J.: Polyarteritis Nodosa: A Clinical and Pathological Study and Report of 6 Cases, *Ann. Int. Med.* 32: 1114 (June) 1950.

THROMBOTIC THROMBOPENIC PURPURA

REPORT OF A CASE

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and

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In 1925 Eli Moschcowitz¹ called attention to a previously undescribed entity of anemia with widespread hyaline thrombosis of capillaries and terminal arterioles. It was not until 1936, however, that Baehr, Klemperer, and Schiffrin² described the pathological picture at post-mortem examination and correlated it with a characteristic clinical syndrome. On histological examination numerous small thrombi were found in the arterioles, capillaries, and venules of almost every organ and tissue. This syndrome was invariably associated with all the usual features of thrombopenia, in addition to an acute febrile episode, severe anemia, and neurological manifestations, which differentiated it from the ordinary type of thrombopenic purpura. Baehr and his associates believed that the lack of platelets in the circulating blood might be due to the myriads of platelets caught in the widespread thrombi in the many small vessels throughout the viscera, so that the available supply was exhausted, resulting in thrombopenia of the peripheral blood.

Subsequent authors³ have described in greater detail the clinicopathological aspects of this singular type of thrombopenic purpura, and increasing awareness of the

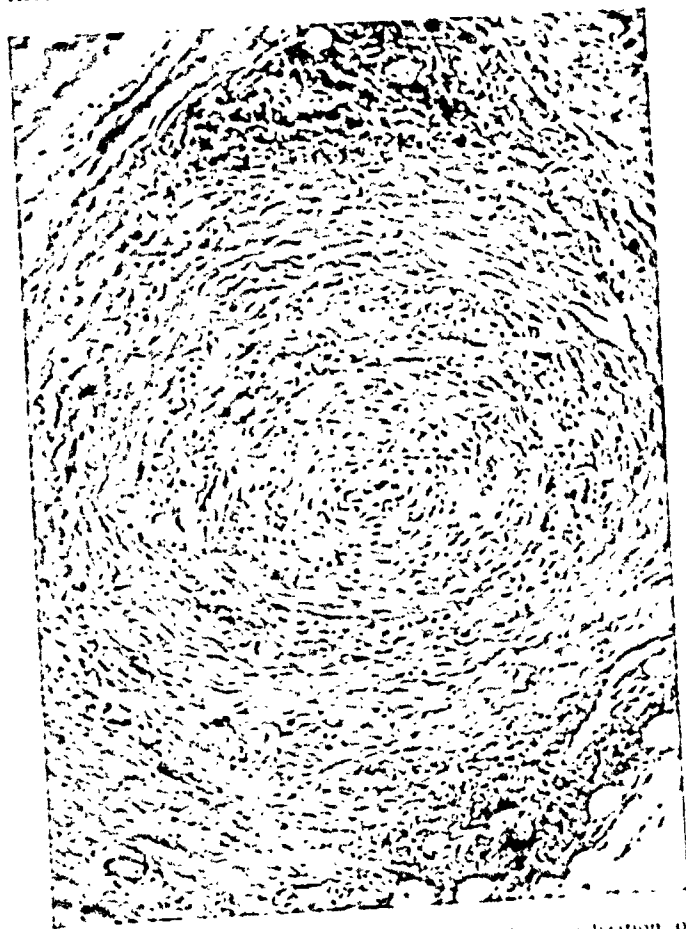


Fig. 5.—State of healing with obliteration and recanalization of the lumen (hematoxylin and eosin $\times 100$).

secondary to ischemic changes may lead to the finding of occult blood in the stools and even to bloody diarrhea. Felsen⁵ stated that diagnosis of polyarteritis may sometimes be made by sigmoidoscopy in instances in which the large bowel is affected. Review of the laboratory data in the case we have described serves to confirm this.

Summarizing the most recent reviews,⁶ we note that clinically, abdominal pain may be a prominent symptom in polyarteritis, occurring in 50% of cases. About 25% of the patients with abdominal pain complain chiefly of pain in the epigastrium. In addition, more than 50% of the patients have sudden onset of disease accompanied by fever, leukocytosis, hypertension, albuminuria, and edema. A lower percentage show dyspnea, nausea, vomiting, weakness, loss of weight, anemia, tachycardia, and arthralgia. The association of such symptoms and signs with emaciation may lead to an erroneous diagnosis of

From the Department of Medicine, Maimonides Hospital.
1. Moschcowitz, E.: An Acute Febrile Pleiochromic Anemia with Hyaline Thrombosis of the Terminal Arterioles and Capillaries, *Arch. Int. Med.* 36: 89 (July) 1925.
2. Baehr, G.; Klemperer, P., and Schiffrin, A.: An Acute Febrile Anemia and Thrombocytopenic Purpura with Diffuse Platelet Thrombosis of Capillaries and Arterioles, *Tr. A. Am. Physicians* 51: 43, 1936.

entity has led to more frequent reports in the medical literature. As the disease has rarely been diagnosed antemortem or preoperatively, the following case identified on clinical grounds and before microscopic section was available may be of interest.

History and Physical Examination.—A 35-year-old white housewife of Italian derivation was admitted to the Maimonides Hospital on Oct. 24, 1949, with the chief complaints of back pain and smoky urine of three weeks' duration. The history of her present illness disclosed that she had enjoyed moderately good health until three weeks prior to admission, when she noted the onset of dull aching pain in the neck, back, and knees, with tenderness of the calves and a pressing pain over the sternum. These symptoms were accompanied by chilly sensations and a temperature of 101 F by rectum. Her attending physician, Dr. Joseph Estrin, treated her symptomatically at that time. An electrocardiogram taken shortly after this was normal. However, in the ensuing two and one-half weeks her symptoms continued, with increasing weakness, anorexia, several episodes of loss of consciousness, and right lumbar pain radiating down both legs. Her urine was grossly bloody and contained numerous white blood cells, albumin, and casts. An intravenous pyelogram was negative. Shortly after this an icteric tinge of the skin was noted but was not accompanied by pruritis. The hemoglobin value was reported at 76%. Seven days before admission the patient had been admitted to another hospital following an episode of loss of consciousness. At this time her hemoglobin value was 38% and the red blood cell count was 1,300,000 cells per cubic millimeter. The bleeding time was 3½ minutes, clotting time 2½ minutes, and there was reticulocytosis, 12%. Several blood smears revealed a complete absence of platelets, but later in her stay adequate platelets were reported as being present. After two blood transfusions she was transferred to the Maimonides Hospital.

Past history was essentially noncontributory, except for an episode of arthritis 12 years previously involving the index and middle fingers of both hands, with occasional swelling and limited motion of the joints over a period of two years. This disappeared spontaneously, and there were no further symptoms until six months prior to the present admission, when she noticed a similar episode of joint swelling for which she was treated with thiamine hydrochloride with a poor therapeutic response. There was no history of exposure to noxious or toxic substances. The family history revealed no similar illnesses or any history of blood dyscrasia. The menstrual history was normal and the patient had delivered two normal full-term babies without complications. She had had no abortions or miscarriages.

Physical examination revealed a temperature of 99 F, a pulse rate of 96, respirations of 24 per minute, and blood pressure of 106/60. She was a well-developed and well-nourished young woman. She was pale and her skin had an icteric tinge. Pertinent physical findings included a marked pallor of the mucous membranes, petechiae in the gums and right buccal mucosa, and several ecchymotic areas of the extremities. The fundi showed numerous small, old, and recent superficial retinal hemorrhages. The heart was not enlarged, and a grade 2 systolic blowing murmur was heard over the entire precordium, with maximal intensity at the pulmonic area. There was no lymphadenopathy, and the liver and spleen were not palpable. There was bilateral costovertebral angle tenderness, more pronounced on the right side.

Laboratory Findings.—On admission, the patient had a red blood cell count of 2,170,000 cells per cubic millimeter, with a hemoglobin value of 9 gm. per 100 cc.; the white blood cell count was 11,500 cells per cubic millimeter, with 55% polymorphonuclear leukocytes, 38% lymphocytes, 2% monocytes, 3% eosinophils, and 1% basophils. Anisocytosis and poikilocytosis of the red blood cells was noted. The platelet count was 27,200 per cubic millimeter. There were 9% reticulocytes. Clotting time was 8 minutes, and the bleeding time was greater than 90 minutes on one occasion and more than 30 minutes several days later. There was no clot retraction in 24 hours. Reaction to a Rumpel-Leede test was highly positive. The red blood cell fragility was normal. Urinalysis showed a specific gravity that

was never higher than 1.015 and proteinuria (1+) with many red blood cells and occasional white blood cells. The urine culture was positive for *Escherichia coli*. Serology was normal, and cold agglutination tests were negative. The heterophil antibody reaction was positive in 1:40 dilution, and the agglutination test for *Trichinella* was strongly positive in a dilution of 1:1280. The antistreptolysin titer was 250 units. A Coombs test was negative, and the blood type was found to be A, M, and Rh positive. The corrected sedimentation rate by the Westergren method was 32 mm. per hour. On admission the fasting blood sugar was 75 mg. per 100 cc., and the blood urea nitrogen 15 mg. per 100 cc., later rising to 53 mg. The blood creatinine was 1.9 mg. per 100 cc., and the total proteins 7.65 gm., with albumin 4.1 gm. and globulin 3.5 gm. per 100 cc. Blood cholesterol was 210 mg. per 100 cc., with 23% free. The serum calcium was 9.6 mg. and phosphorus 2.7 mg. per 100 cc. The alkaline phosphatase was 3.2 King-Armstrong units. The icterus index was 10.2 units and later rose to 16.1 units. The cephalin flocculation was 4+ on several occasions and the thymol turbidity 15 units. The electrocardiogram showed slight depression of the S-T segment in lead I with changes in the T waves in leads I and 2 and in V₁ through V₆. A subsequent tracing showed normal S-T segments and decreased changes in the T waves. A bedside chest roentgenogram showed shading of both lower lung fields and later a "left pleural effusion." Sternal marrow aspiration showed a normal number of megakaryocytes, with few platelets and active erythropoiesis.

Hospital Course.—The patient's hospital course was unremarkable until the second hospital day, when her regular menstrual period began. The bleeding, however, was unusually severe; a blood transfusion was attempted but, after 250 cc. had been given, was discontinued because of a rise in temperature to 104 F. The stool, which had been normal, was now found to be grossly bloody. The next two days were marked by profuse vaginal bleeding and periodontal hemorrhage, with a drop in hemoglobin to 6 gm. per 100 cc. Because of the blood picture and shock-like state, the patient was treated with testosterone in the hope of decreasing the menstrual flow. Oxygen was given by mask, saline and glucose were given intravenously, and 2,500 cc. of blood was administered during the next 48 hours. During this time a prolonged rise in temperature to 102 F was noted and was thought to be due primarily to transfusion reactions. Two blood cultures were sterile, and the urine culture showed the presence of *E. coli*. A throat culture showed only *Staphylococcus aureus* and diphtheroids. By the fifth day of hospitalization the examination of the chest showed signs of consolidation in the lower left and upper right lobes. The patient was given 1,000,000 units of penicillin every three hours and 1 gm. of streptomycin every six hours.

With recovery from her shock-like state the patient remained confused, irritable, and at times disoriented. The consultant in hematology (J. W.) felt that the presence of previous fever without known bacteriological cause, the hemolytic anemia, and

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the intestine showed evidence of infarction which gave the appearance of mucosal ulcers. Most recently, Sandler and associates,⁴ described a case of polyarteritis with pulmonary cavitation. They casually referred to the concomitant presence of several superficial ileal ulcerations measuring up to 4 by 1.5 cm.

The literature concerned with polyarteritis abounds with reports on the incidence of coexistent abdominal symptoms and gross vascular lesions, but only sporadic mention is made of the simultaneous presence of intestinal ulceration. Pathologically, the intestinal lesions vary from solitary, minute, isolated foci to confluent and massive ulceration. Acute involvement of the stomach or bowel wall may lead to perforation, and fatal peritonitis. The submucous and muscular coats are affected initially, but later erosion and ulceration of the overlying mucosa

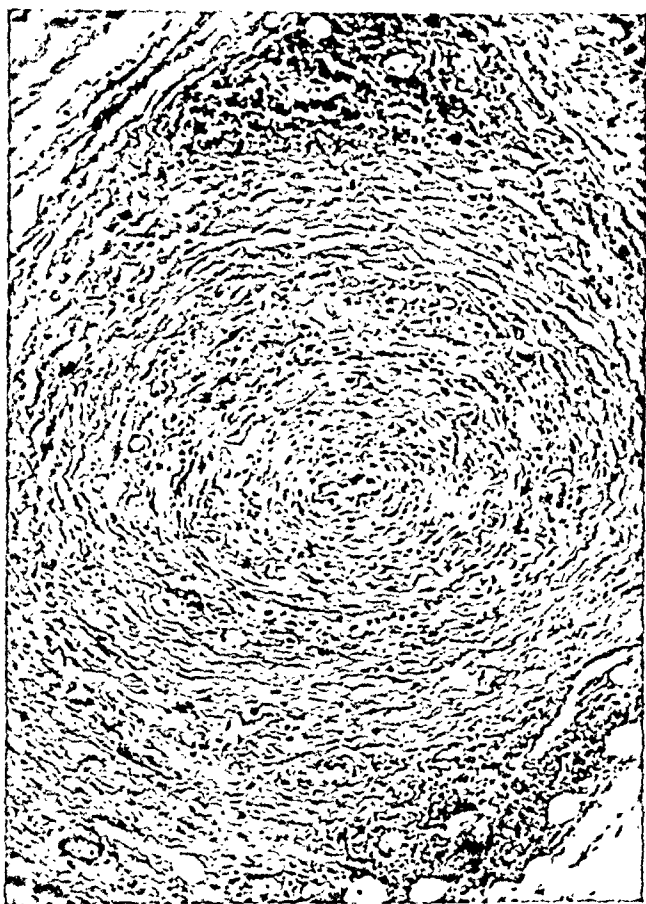


Fig. 5.—Stage of healing with obliteration and recanalization of the men (hematoxylin and eosin $\times 100$).

secondary to ischemic changes may lead to the finding of occult blood in the stools and even to bloody diarrhea. Felsen⁵ stated that diagnosis of polyarteritis may sometimes be made by sigmoidoscopy in instances in which the large bowel is affected. Review of the laboratory data in the case we have described serves to confirm this.

Summarizing the most recent reviews,⁶ we note that clinically, abdominal pain may be a prominent symptom in polyarteritis, occurring in 50% of cases. About 25% of the patients with abdominal pain complain chiefly of pain in the epigastrium. In addition, more than 50% of the patients have sudden onset of disease accompanied by fever, leukocytosis, hypertension, albuminuria, and edema. A lower percentage show dyspnea, nausea, vomiting, weakness, loss of weight, anemia, tachycardia, and arthralgia. The association of such symptoms and signs with emaciation may lead to an erroneous diagnosis of

carcinoma of the stomach or of the gastrointestinal tract. It is not uncommon for the patient to exhibit signs of intestinal obstruction as a terminal event. Thus, in retrospect, it is apparent that the case here presented was typical of polyarteritis.

SUMMARY

Acute ulcerative enteritis resulted from vascular thrombosis secondary to the inflammatory changes in the small arteries and arterioles. The diagnosis, which had completely baffled the clinicians, was made after microscopic examination of tissue secured at autopsy. From a study of this and other cases, it is apparent that polyarteritis is an occasional cause of intestinal ulceration.

U. S. Naval Hospital, Beaufort.

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THROMBOTIC THROMBOPENIC PURPURA

REPORT OF A CASE

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Burton M. Cohen, M.D.

and

Janet Watson, M.D., Brooklyn

In 1925 Eli Moschcowitz¹ called attention to a previously undescribed entity of anemia with widespread hyaline thrombosis of capillaries and terminal arterioles. It was not until 1936, however, that Baehr, Klemperer, and Schiffrin² described the pathological picture at post-mortem examination and correlated it with a characteristic clinical syndrome. On histological examination numerous small thrombi were found in the arterioles, capillaries, and venules of almost every organ and tissue. This syndrome was invariably associated with all the usual features of thrombopenia, in addition to an acute febrile episode, severe anemia, and neurological manifestations, which differentiated it from the ordinary type of thrombopenic purpura. Baehr and his associates believed that the lack of platelets in the circulating blood might be due to the myriads of platelets caught in the widespread thrombi in the many small vessels throughout the viscera, so that the available supply was exhausted, resulting in thrombopenia of the peripheral blood.

Subsequent authors³ have described in greater detail the clinicopathological aspects of this singular type of thrombopenic purpura, and increasing awareness of the

From the Department of Medicine, Maimonides Hospital.

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SICKLE CELL ANEMIA IN A WHITE ADULT

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Three cases of sickle cell anemia have been reported previously in Greece, but no instance in which the disease occurred in a white person in any other country is mentioned in the European literature. It is believed that the disease occurs in Greece in a mild form. A fourth case of sickle cell anemia in a white adult is reported.

REPORT OF A CASE

The patient, a 30-year-old Greek army officer, was admitted to the hospital complaining of weakness, languor, faintness, vertigo, and palpitations. His parents were healthy, with normal blood cell counts, blood bilirubin, Wassermann reactions, and absence of sickle cells in staining tests. A maternal uncle who is suffering from chronic malaria with anemia could not be contacted for a blood test.

The disease started in early childhood. The skin and sclerae had a permanent yellow tint. Crises had occurred frequently and periodically, with pain in the long bones, joints, and waist

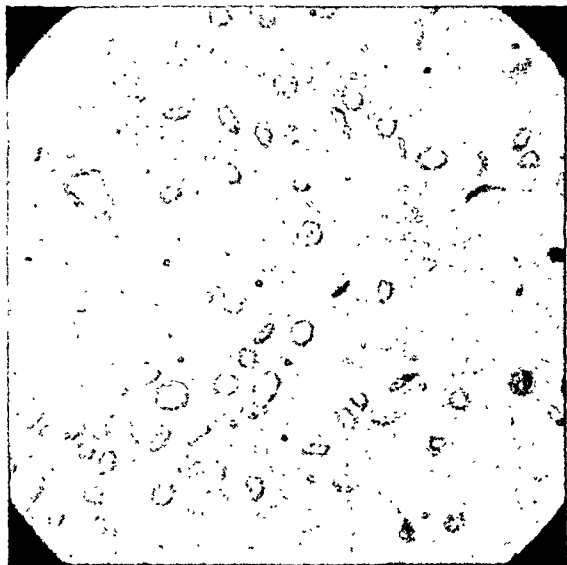


Fig. 1.—Photomicrograph showing target cells during an acute attack.

followed by a rise in temperature, accentuation of the yellow tint of the skin and sclerae, enlargement of the spleen, hyper-colored urine, and great decrease in erythrocyte count and hemoglobin value. The patient had been treated in hospitals in Greece and Brussels with a diagnosis of typical hemolytic jaundice.

Laboratory Examinations.—The hemoglobin value was 70%. There were 4,580,000 erythrocytes and 14,000 leukocytes with 73% mature and 1% immature neutrophils, 2% eosinophils, and 24% lymphocytes. There was slight anisocytosis and poikilocytosis, and a few sickle cells appeared after staining. The platelet count was 250,000. The fragility of the erythrocytes was within normal limits (0.35 to 0.23% sodium chloride solution). The sedimentation rate was 4.5 mm. per hour (Westergren). Bleeding and coagulation times were normal. The retractility of the clot was normal. The blood group was O. The prothrombin time was 11 seconds with 100% concentration. The serum bilirubin was 0.15 mg. per 100 cc. by indirect reaction (Van den Bergh). The serum cholesterol was 0.166 gm. per 100 cc. and the serum albumin 0.68 per 100 cc. The Kahn test was negative. The bone marrow contained 15% myelocytes, 9% metamyelocytes, 3% eosinophils, 24% polymorphonuclears, 9% lymphocytes, and 35% normoblasts.

The urine contained slightly abnormal amounts of urobilin and urobilinogen. There was no albumin, sugar, bile pigment, hemoglobin, hemosiderin, or Bence-Jones protein.

X-ray examinations showed the chest, heart, alimentary tract, and gallbladder to be normal. The long bones showed narrowing of the medullary cavity, with periosteal reaction and irregular trabeculations. The short and flat bones showed slight exaggeration of trabecular markings of the ilia and phalanges with cortical thinning. A roentgenogram of the skull showed widening of the diploe, thinning of the outer tables, and mottling of trabeculae.

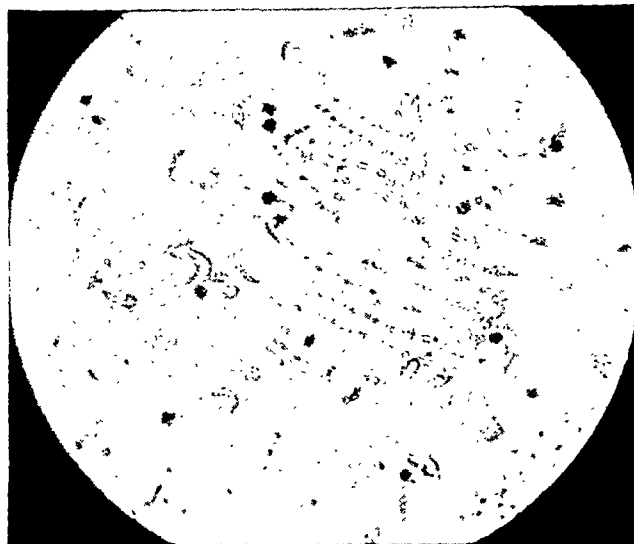


Fig. 2.—Photomicrograph showing sickle cells during an acute attack.

An electrocardiogram indicated normal function. On the 10th day the patient's temperature rose to 103 F, and this was followed by severe pains in the waist, joints, and bones, especially of the limbs. This situation lasted for about four days with weakness and pallor remaining. Blood tests showed a decrease of erythrocytes in four days from 4,500,000 to 1,700,000 and hemoglobin to 30%. There were 70,000 leukocytes, with 1% myeloblasts, 1% promyelocytes, 16% myelocytes, 21% meta-

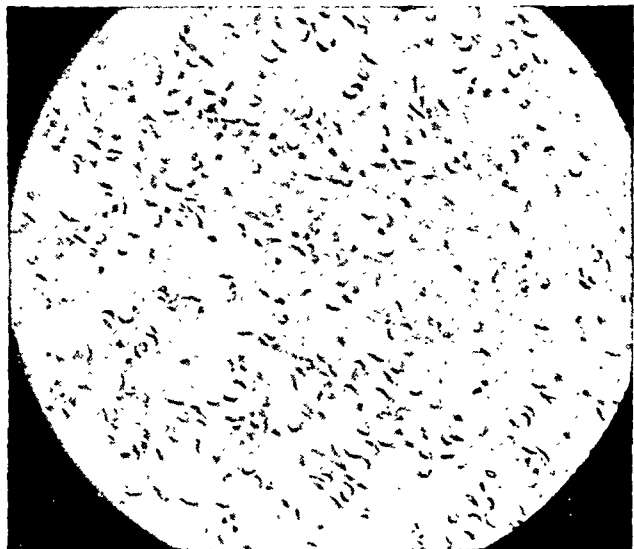


Fig. 3.—Photomicrograph showing increase in sickle cells after specimen was allowed to stand.

myelocytes, 47% polymorphonuclears, 12% lymphocytes, 2% basophilic normoblasts, and 22% reticulocytes. The fragility of the erythrocytes was 0.36 to 0.25% sodium chloride solution. The blood bilirubin increased from 0.15 to 0.60 mg. per 100 cc. The bone marrow contained 3% myeloblasts, 2% metamyelocytes, 17% polymorphonuclears, 6% rhabdocytes, 2% lymphocytes, 10% prenormoblasts, 45% basophilic normoblasts, 10% polychromophylic normoblasts, and 5% oxyphilic normoblasts. The urine test for urobilinogen was slightly positive, while tests

for hemoglobin and hemosiderin were negative. Morphological inspection of erythrocytes showed target cells and sickle cells in proportion of 7 to 20% (Fig. 1 and 2). In tests producing sickle cells, the proportion of sickle cells reached 70% (Fig. 3). Physical examination showed no changes except accentuation of the yellow tint of sclerae and skin and slight enlargement of the spleen and liver.

A gradual recovery started on the sixth day from the onset of the crisis and was complete in about 25 days.

COMMENT

A case of sickle cell anemia in a white adult is described. It is the fourth case to be reported in Greece. Two reports have been published by Dr. Makrycostas¹ of patients treated in Evangelismos Hospital, Athens. Another case has been reported recently (April, 1950) to the Athens Medical Association by D. Komninos, D. Bakalos, and P. Katsiroumbas. No case was mentioned in the European literature. Therefore, I conclude that, although this disease is rarely seen in Greece, it does exist in persons in whom no Negro blood is suspected. Bakalos and Katsiroumbas believe that sickle cell anemia may be included in the Mediterranean hemopathic syndromes.^{1a} Attention is called to the fact that during the crisis the decrease of erythrocytes (to 1,700,000) was not followed by proportionate hyperbilirubinemia. Blood bilirubin never exceeded 0.60 mg. per 100 cc. and remained at the same level until complete clinical recovery. This justifies Dr. Dameshek's² opinion that hemolysis in this disease must be considered as secondary. On the other hand, there is no hyperbilirubinemia, because the liver is healthy enough to provide complete metabolism of the slowly produced bilirubin. Taking into consideration the lack of certain clinical symptoms and its long duration, I conclude that sickle cell anemia is seen in Greece in a mild or degenerated form.

74 3rd September St.

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DUODENAL OBSTRUCTION DUE TO PRESSURE OF SUPERIOR MESENTERIC VESSELS

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Chronic obstruction of the duodenum is a condition rarely encountered in adults, though an occasional case of obstruction due to pressure by the superior mesenteric vessels appears in the literature.¹ It is entirely possible that this obstruction is brought about by numerous factors, such as (1) the branching of the superior mesenteric artery off the aorta in an unusually low position, (2) a short vessel, or (3) visceroptosis. The condition is natu-

rally not found in quadrupeds, because in them the mesentery is directed ventrally, whereas in man it is directed caudally. Today, with adequate roentgenologic aid, this condition is a recognized clinical and pathological entity, and its correction in most cases is satisfactorily accomplished by surgery.

REPORT OF A CASE

Patient S. S., a 66-year-old white woman, was admitted to the St. Joseph Hospital on the service of Dr. Fred W. Rankin with the chief complaint of weakness of six months' duration and vomiting of two days' duration. She stated that she had been exceptionally thin all her life, and that during the five years preceding admission her weight had ranged between 72 and 80 lb. (32.7 and 36.3 kg.). Six months before admission she began to have increasing weakness, and 11 weeks before admission the weakness became so severe that she remained in bed most of the time. Two days before admission she began to have severe vomiting, which persisted till she was admitted to the hospital. Neither nausea nor pain was associated with the vomiting. She



Roentgenogram one hour after the ingestion of barium showing obstruction of third part of duodenum.

had lost 7 lb. (3.2 kg.) since the onset of the weakness and on admission weighed 65 lb. (29.5 kg.).

On physical examination the only remarkable finding, in addition to the extreme emaciation, was an outpouching on the left side of the abdomen extending from the left upper quadrant to the left lower quadrant. A succussion splash could easily be elicited over this outpouching. Routine blood cell counts, blood urea nitrogen, total proteins, albumin, globulin, and albumin globulin ratio were normal. A flat film of the abdomen showed a markedly dilated stomach extending down to the crest of the ilium. A Levin tube was anchored, and 1,600 cc. of greenish fluid was removed during the next few hours.

A tentative diagnosis of pyloric obstruction was made. The patient was given fluids and vitamins parenterally and gastric lavage three times a day. Two days later roentgenologic examination of the stomach and duodenum showed the pylorus to be open and an obstruction to be at the third part of the duodenum. The obstruction appeared to result from pressure outside the bowel. Two days later laparotomy revealed a moderately dilated stomach and pylorus and distended duodenum up to the point at which the duodenum was crossed by the superior mesenteric vessels. Distal to this, the small bowel was collapsed. The region between the dilated duodenum and collapsed jejunum was thor-

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oroughly explored. No growth or other cause for the obstruction was found, except the superior mesenteric vessels. The collapsed jejunum was opened and a finger introduced into the lumen back into the dilated duodenum. Nothing was in the lumen, and the obstruction was obviously at the passage of the superior mesenteric vessels across the duodenum.

Gastrojejunostomy, duodenojejunostomy, and even division of the duodenum with anastomosis of the two limbs in front of the root of the mesentery have all been advocated as the proper surgical procedure for treatment of this condition. Any procedure which reroutes the food around the site of obstruction should be satisfactory, however, and in this case a gastrojejunostomy was done, because it could be accomplished more easily and quickly than either of the other procedures.

The postoperative course was uneventful, and, by the 10th postoperative day, the patient was ambulatory and feeling much better than she had for 11 weeks before surgery. Follow-up six months later revealed that her weight had returned to what it had been for the five years prior to hospitalization; her usual routine of living had been reestablished, and she had had no further attacks of vomiting.

SUMMARY

A case of obstruction of the distal part of the duodenum by the superior mesenteric vessels, producing dilatation of the stomach and vomiting is reported. The condition was relieved by gastrojejunostomy.

544 W. Second St.

MASCULINOVOBLASTOMA OR MASCULINIZING ADRENAL REST TUMOR OF OVARY

REPORT OF A CASE

Jonathan E. Rhoads, M.D.

Harold A. Zintel, M.D.

and

Robert C. Horn Jr., M.D., Philadelphia

Tumors of the ovary that cause symptoms related to the endocrine system include arrhenoblastoma, masculinoblastoma, often called the adrenal rest tumor, and luteinized tumors, variously called luteomas, luteinomas, and luteinized granulosa cell or theca cell tumors. The two that result in symptoms of masculinization are arrhenoblastoma and masculinoblastoma. Arrhenoblastomas are somewhat commoner, 94 having been reported in 1947 by Iverson.¹ Masculinoblastomas are rarer. Iverson limited the reported cases to 15 definitely established, after excluding six cases in which the patients did not have complete masculinization associated with a lipoid cell tumor of the ovary.

The origin of lipoid cell tumors is disputed, some authors believing that they arise from adrenal rests and some believing that they arise from undifferentiated cells in the ovary, while still others believe that both modes of origin are possible. Histologically, these tumors resemble adrenal cortical tissue. According to Curtis,² this group of tumors may produce hypertension and glucosuria-

symptoms also observed in certain cases of adrenal cortical tumors and pituitary tumors, but not with arrhenoblastomas.

The following report describes a case of masculinoblastoma. This patient exhibited a marked degree of masculinization but no hypertension and glucosuria. Follow-up observations extended over five and a half years.

REPORT OF A CASE

Mrs. M. F. a 37-year-old white woman, was admitted to the Hospital of the University of Pennsylvania on Sept. 9, 1944, because of "dizzy spells and falling hair." She stated that she had been well until eight years before admission, when she had a baby that died 24 hours after its birth. After the birth of this baby, her menstrual periods appeared at the usual 28-day intervals. However, the amount of flow gradually decreased until she ceased to menstruate four years before admission to the hospital. The breasts had gradually become smaller. For seven years she had been losing the hair on her head, and coarse hair had appeared on her face, chest, arms, legs, and lower abdomen. She had not had her hair cut for eight years. She wore a wig and had to shave every other day. During the eight years her voice had become deep and "husky." Three months before admission she



Fig. 1.—Left ovary removed at operation. Tumor tissue has replaced the greater part of the gland. Residual ovarian tissue surrounds the tumor.

began to have "dizzy spells." The dizziness appeared when she bent forward and then suddenly straightened up. During other activities she had no dizziness. There was no history of visual changes. Her weight had remained constant for the past eight years. Her sexual reactions had not changed. There was a history of frontal headaches occurring about once every two weeks since childhood.

The patient's physique was decidedly masculine. The arms and legs were firm and muscular. The texture of the skin of the entire body was quite coarse. The complexion of the skin of the face was described as ruddy. There was no evidence of abnormal fat distribution or striae. There was coarse straight hair on the chest, face, abdomen, and extremities, and the pubic hair had the inverted triangle distribution characteristic of the male. There was little hair from the occiput to the forehead. The remaining hair around the sides of the scalp was sparse, thin, and dry. The blood pressure was 135/80. No abdominal masses were palpable. Pelvic examination did not disclose any abnormalities. The clitoris was not enlarged and the remaining external genitalia were normal.

At operation on Sept. 27, 1944, the left ovary was found to be enlarged and the right ovary was small (1 by 1 by 1.5 cm.). A frozen section of a biopsy of the left ovary was reported by the pathologist as showing tumor tissue. The entire left ovary was removed (Fig. 1). After removal of the ovary a small mass was palpated above the superior pole of the left kidney, and

From the Harrison Department of Surgical Research, School of Medicine, University of Pennsylvania, the Departments of Surgery and the Laboratory of Surgical Pathology, Hospital of the University of Pennsylvania.

1. Iverson, L.: Masculinizing Tumors of Ovary: Clinico-Pathologic Survey with Discussion of Histogenesis and Report of 3 Cases, *Surg., Gynec. & Obst.* 84: 213, 1947.

2. Curtis, A. H.: Origin of Adrenal-like Tumor of Ovary (Hypernephroma of Ovary, Adrenal Tumor of Ovary, Masculinoblastoma, Luteoma, Luteinoma), *Am. J. Obst. & Gynec.* 52: 115, 1946.

therefore the low midline incision was closed and a left sub-costal incision was made to explore the adrenal area. The mass removed from this area proved to be an accessory spleen. Her postoperative course was uneventful and she was discharged from the hospital on the 14th postoperative day.

Pathological Report.—The specimens were an ovary and an accessory spleen. The ovary measured 3 by 2 by 1.5 cm. It was composed of soft brown tissue enclosed by a tough capsule of what appeared to be ovarian stroma. A portion of this lesion had been removed previously for biopsy and on frozen section appeared to be a tumor of undetermined nature. The accessory spleen was 1.3 cm. in diameter. The specimens were fixed with Bouin's fluid.

Microscopic examination confirmed the diagnosis of an accessory spleen. Numerous sections of the ovary all showed similar structures. There was a rim of compressed stroma about the periphery, which contained a number of primordial follicles and corpora albicantia, none of which were active. The remainder of the ovary was occupied by the tumor, which was fairly well circumscribed although it lacked a distinct capsule (Fig. 2). The tumor presented a fairly uniform picture. The cells had considerable amounts of clear cytoplasm, not infrequently containing pink-staining granules. The nuclei varied somewhat in size but were regular and round or oval. No nuclear changes suggested malignant disease, and mitotic figures were not seen. The cells were arranged in cords like the cells of endocrine glands. The stroma was fairly abundant but was delicate and apparently markedly edematous. The tumor was fairly vascular, many of the vessels showing degenerative changes. There were numerous hemorrhages. These were not the signs of arrhenoblastoma, but

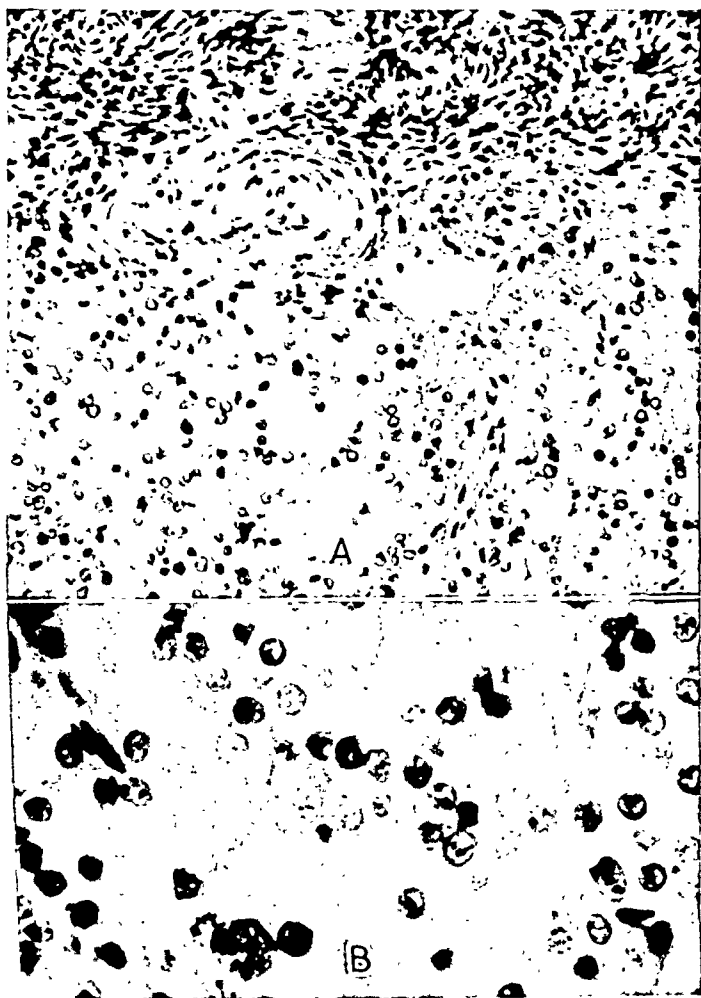


Fig. 2.—Photomicrographs of sections of the left ovary. *A*, a thin layer of ovarian stroma is shown at the top and tumor cells at the bottom. Hematoxylin-eosin stain ($\times 175$). *B*, the tumor cells, arranged in cords, have abundant finely granular or vacuolated cytoplasm. There is considerable nuclear variation.

of another group of masculinizing ovarian tumors best known as adrenal rest tumors. The diagnosis was (1) adrenal rest tumor with masculinization, and (2) accessory spleen.

Postoperative Course.—Within 30 days of the operation the patient began to menstruate and noticed that her voice was

higher in pitch. Within three months she was having menstrual periods similar to the ones she had had prior to her illness. The menstrual periods appeared regularly every 25 days, lasted for four days, and required approximately four pads per day. There was little pain. At this time it was noticed that the hair on the head was increasing and that generally the body hair was decreasing. At the end of one year the facial hair had disappeared to the



Fig. 3.—*A*, photograph of patient immediately before operation. *B*, photograph of patient five and one-half years after operation.

extent that she shaved only once in three weeks. She had been gaining weight and was feeling very well. Two years after operation she noted that her breasts were becoming larger and that her voice was more normal. Three years after operation it was noted that the amount of hair on her head was still increasing slowly, and it was necessary to have her hair trimmed occasionally. She had not worn a wig for one year. The hair on her face had almost completely disappeared. The only portion of her face that required shaving was a small area just beneath the chin that had to be shaved approximately once a week.

During the five and one-half year period of observation her menstrual periods have remained regular except on two occasions. The first of these was three years postoperatively when she had no menstrual flow for three months. The patient at that time thought she had a miscarriage, but there was no clinical evidence such as the passing of tissue to support such a diagnosis. The menstrual periods were then normal until 4 years postoperatively, when menstrual bleeding appeared 3 days before the expected time, followed by a second period of bleeding 13 days later. Pelvic examination at this time did not reveal any clinical evidence of pregnancy or any evidence of recurrence of the tumor. The patient's appearance before operation and five and one-half years afterward is shown in Figure 3.

SUMMARY

A case of masculinovoblastoma (adrenal rest tumor of the ovary) in a patient who has been followed for five and one-half years is reported. Surgical excision of the tumor was followed by restoration of menses, regression of baldness, regression of facial hair, and regression of other symptoms of masculinization.

3400 Spruce St. (Dr. Rhoads).

Tuberculous Lymphadenitis.—Chemotherapy, notably with streptomycin and para-aminosalicylic acid (PAS), is a fairly recent and valuable addition to the therapy of tuberculous lymphadenitis but the wave of enthusiasm it has evoked in this connection is not justified by the results. Antimicrobial drugs have their chief effect on the early, exudative form of the disease and have little value in the treatment of caseous foci or cold abscesses. However, chronic tuberculous sinuses do respond well to antimicrobial therapy.—Charles W. Lester, M.D., *Lymph Node Tuberculosis and Its Treatment in Accessible Nodes*, *The American Review of Tuberculosis*, December, 1951.

COUNCIL ON PHYSICAL MEDICINE AND REHABILITATION

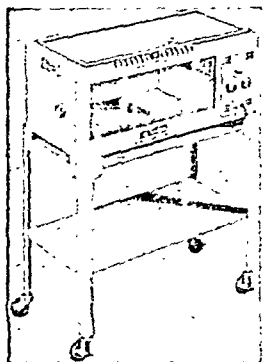
The Council on Physical Medicine and Rehabilitation has authorized publication of the following reports.

RALPH E. DE FOREST, M.D., *Secretary.*

ARMSTRONG X-P EXPLOSION-PROOF BABY INCUBATOR, MODEL 22, ACCEPTED

Manufacturer: The Gordon Armstrong Company, Inc., 1501 Euclid Ave., Cleveland 15, Ohio.

The Armstrong X-P Explosion-Proof Baby Incubator, Model 22, is a device for housing an infant under conditions of regulated temperature, humidity, and oxygen flow. The enclosure for the infant has a transparent front and top, so that the occupant can be watched from a distance.



Armstrong X-P Explosion-
Proof Baby Incubator,
Model 22

The incubator proper is mounted on a stand with casters, so that it can be moved about on the floor when not kept on a table. It has connections for oxygen, and for operation it requires a source of 60-cycle alternating current at 110 to 115 volts. It draws 162 watts. It is listed by Underwriters' Laboratories, Inc. Its distinctive feature is an explosion-proof heating unit, in which all electric wiring, switches, and controls are sealed with copper-riveted seals.

The incubator stand and the cabinet for accessories are not included in the dimensions and weights which follow. The incubator proper measures 35 (height) by 81 by 38 cm. (13¾ by 32 by 15 in.) and weighs 25.4 kg. (56 lb.). Packed for shipment it measures 42 by 84 by 48 cm. (16½ by 33 by 19 in.) and weighs 32 kg. (71 lb.). The foreign shipping weight is 32 kg.

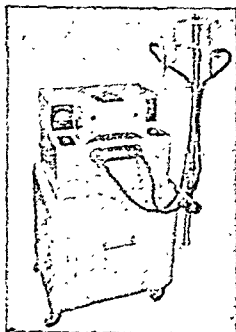
Evidence from practical tests under conditions acceptable to the Council indicated that the apparatus was sound in construction, convenient as an incubator, and safe in operation when properly grounded. The Council on Physical Medicine and Rehabilitation voted to include the Armstrong X-P Explosion-Proof Baby Incubator, Model 22, in its list of accepted devices.

MASTER FISCHERTHERM DIATHERMY, MODEL 1200, ACCEPTED

Manufacturer: R. A. Fischer & Company, 517 Commercial Street, Glendale 3, Calif.

The Master Fischertherm Diathermy, Model 1200, is a device for generating short wave medical diathermy at a frequency of 27.120 megacycles. It has the F.C.C. Type Approval No. D491.

The apparatus is housed in a cabinet that rolls on casters on the floor. The over-all dimensions of the apparatus are 98 (height) by 60 by 46 cm. (38½ by 23¾ by 18 in.) and its net weight is 59 kg. (131 lb.). Packed for shipment it requires two crates, each measuring 67 by 60 by 56 cm. (26½ by 23½ by 22 in.) and weighing together 93 kg. (205 lb.). The apparatus comes with or without a hinged arm applicator. Accessories include a line cord and an operating instruction sheet. Evidence of satisfactory construction and satisfactory operation was obtained from sources acceptable to the Council. The Council on Physical Medicine and Rehabilitation voted to include the Master Fischertherm Diathermy, Model 1200, in its list of accepted devices.



Master Fischertherm Dia-
thermy, Model 1200

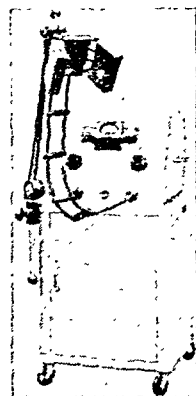
BIRTCHER CHALLENGER SHORT-WAVE DIATHERMY, NO. 850, ACCEPTED

Manufacturer: The Birtcher Corporation, 4371 Valley Blvd., Los Angeles 32.

The Birtcher Challenger Short-Wave Diathermy, No. 850, is designed to produce a "tube-generated" current for use both in medical diathermy and in minor electrosurgery. It can either be set on a table or mounted on a sub-cabinet. The latter is provided with casters and can be moved about on the floor. The apparatus generates electromagnetic waves of a frequency of 27.12 megacycles, corresponding to a wavelength of 11 m. It has Type Approval No. D-529 of the Federal Communications Commission and is listed by Underwriters' Laboratories, Inc.

It is 38 cm. high (15 in.) and has a sloping front panel; its base measures 58 by 41 cm. (23 by 16 in.). It weighs 27 kg. (60 lb.). Packed for shipment it measures 46 by 71 by 48 cm. (17¾ by 28 by 19 in.) and weighs 38 kg. (85 lb.). It requires a 60-cycle alternating current at 110 to 112 v. and draws 650 watts.

The Council on Physical Medicine and Rehabilitation voted to include the Birtcher Challenger Short-Wave Diathermy, No. 850, in its list of accepted devices.

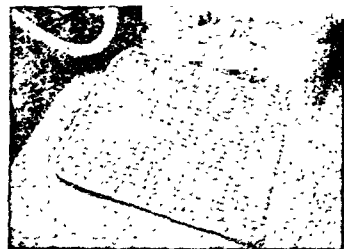


Birtcher Challenger
Short-Wave Diathermy
No. 850

SACRO-EASE, MODELS "R" AND "200," ACCEPTED

Manufacturer: McCarty's, 2024 San Pablo Ave., Oakland, Calif.

The Sacro-Ease is a seating pad marketed in several different forms. The principle, as indicated by a diagram in the advertising folder supplied by the manufacturer, is simply a stiffening of the seat (analogous to the placing of a board under a mattress). The diagram shows that in some seats there is a yielding of the central areas, with the result that most of the weight of the trunk is borne on the tubera ischiadica; the diagram also shows very well the resulting tendency of the body to slide forward on the seat, so that constant muscular effort is needed to keep a person in place. The diagram shows that a more rigid seat redistributes the pressures in a way that must sometimes be distinctly beneficial, and must help to overcome the tendency to slide forward. The manufacturer claimed that this device, used on the seat of an automobile, frequently relieved the fatigue and pain in the back experienced by some drivers.



Sacro-Ease

Two forms were submitted by the manufacturer. Model "R" is simply a seat, small enough to lay on an automobile seat and measuring 48 by 36 cm. (19 by 14 in.). Unpacked it weighs 1.3 kg. (2 lb. 3 oz.); the shipping weight is 1.5 kg. (3 lb. 8 oz.). Model "200" is the same seat with added hinged back rest; its shipping weight is 2.9 kg. (6 lb. 6 oz.). It is made with a thin, flat, tool-steel frame; suspension is obtained by a one-piece latex rubber sleeve, formed with a series of strips under tension to help support the body.

The Council obtained evidence indicating that this device gave symptomatic relief when ordered by physicians in certain cases of lumbosacral, sacroiliac, and sciatic discomfort, and that the manufacturer's claim that this device gave increased comfort to some patients was well founded.

The Council on Physical Medicine and Rehabilitation voted to include the Sacro-Ease, Models "R" and "200," in its list of accepted devices.

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PROPHYLAXIS OF INFLUENZA

The possibility of developing an adequate vaccine against all types of influenza has been viewed with some pessimism since 1947. During the influenza epidemics of 1943 and 1945 a standard vaccine made from the two immunologically distinct types of influenza virus (types A and B) provided significant protection against the disease,¹ but in the 1947 epidemic this vaccine proved completely ineffective.² When it was discovered that the 1947 epidemic was due to a mutant strain of type A virus (type A') and when other immunologic variants of the virus were encountered in different parts of the world, it was predicted in some quarters that the virus would prove capable of an infinite number of mutations and that vaccine prophylaxis of influenza would therefore be impractical. Since each new epidemic might conceivably be due to a new mutant strain, vaccine prepared from previously identified strains would be ineffective. Moreover, vaccines prepared from the new strain after the onset of an

epidemic might not be available in quantity lots before the epidemic had spent itself, since it is estimated that from 5 to 30 weeks would be required for the mass production of a new influenza vaccine.

This pessimistic outlook has not been shared by all workers, however. Salk and associates³ of the University of Pittsburgh believe that the weight of the evidence is against the concept of continuous or infinite variation in the virus of human influenza. Since the discovery of the virus 19 years ago, only two completely distinct immunologic types (A and B) have been identified, and the antigenic variants of these types encountered in the laboratory or in nature differ only in a limited degree from the parent cultures. Thus it should be possible to select a group of strains with antigenic properties covering the entire range of the known influenza A and B viruses and to incorporate them in a vaccine that would give adequate protection against all or most of the naturally occurring strains. Serologic studies by these workers with recently isolated strains suggest that this may be accomplished without great difficulty. If such vaccines can be prepared they will represent a notable step forward in this field. In the meantime, the currently available commercial vaccine as licensed by the National Institutes of Health offers some protection against infection with the strains of the virus incorporated in the vaccine.

Vaccines with broad antigenic coverage will not solve the problem of influenza prophylaxis completely, however. Methods must be found to enhance the degree and duration of the immunity produced by the inactivated virus. Vaccination as currently practiced does not provide complete protection for all persons, and the immunity produced lasts only a few months. A number of investigators have attempted to increase the efficiency of the vaccine by using multiple inoculations,⁴ increasing the concentration of the virus,⁵ or administering it by different routes.⁶ Their efforts have met with varying success. Interesting results have been obtained by the use of a vaccine emulsified in mineral oil.⁷ This type of vaccine induces antibody titers that are higher and that remain elevated for longer periods than those induced by ordinary vaccine. The local inflammatory reactions encountered by the early users of this technique are reported to have been eliminated by the use of a lighter mineral oil, a different emulsifying agent, and intramuscular rather than subcutaneous injections.⁸ Another method that has been shown to increase the effectiveness of subcutaneous vaccine with type A virus is the simultaneous intranasal administration of type B virus.⁹ This work, which was done on mice, awaits clinical confirmation in man.

A somewhat different approach to the prophylaxis of influenza has been suggested by Andrewes.⁹ This involves the application of the interference phenomenon in virology. It is known that certain viruses will interfere with or suppress the activities of other viruses inoculated at the same time or shortly before. Employing this principle, Andrewes has been able to prevent the development of clinical influenza in ferrets following intranasal inoculation of virulent type A influenza virus by inoculating the same animals one to three days earlier with attenuated type B virus. Although these animals subsequently become immune to both viruses, the initial inhibiting effect is not due to immunity, for, if the interval

1. Members of the Commission on Influenza, Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army, Preventive Medicine Service, Office of the Surgeon General, United States Army: A Clinical Evaluation of Vaccination Against Influenza: Preliminary Report, *J. A. M. A.* 124:982 (April 1) 1944. Francis, T., Jr.: The development of the 1943 Vaccination Study of the Commission on Influenza, *Am. J. Hyg.* 42:1 (July) 1945. Francis, T., Jr.; Salk, J. E., and Brace, W. M.: The Protective Effect of Vaccination Against Epidemic Influenza B, *J. A. M. A.* 131:275 (May 25) 1946. Hirst, G. K.; Vilches, A.; Rogers, O., and Robbins, C. L.: The Effect of Vaccination on the Incidence of Influenza B, *Am. J. Hyg.* 45:96 (Jan.) 1947.

2. Francis, T., Jr.; Salk, J. E., and Quilligan, J. J., Jr.: Experience with Vaccination Against Influenza in the Spring of 1947: A Preliminary Report, *Am. J. Pub. Health* 37:1013 (Aug.) 1947. Sigel, M. M., and others: Influenza A in a Vaccinated Population, *J. A. M. A.* 136:437 (Feb. 14) 1948. Loosli, C. G.; Schoenberger, J., and Barnett, G.: Results of Vaccination Against Influenza During the Epidemic of 1947, *J. Lab. & Clin. Med.* 33:789 (July) 1948.

3. Salk, J. E.; Laurent, A. M., and Bailey, M. L.: Direction of Research on Vaccination Against Influenza—New Studies with Immunologic Adjuvants, *Am. J. Pub. Health* 41:669 (June) 1951.

4. Beveridge, W. I. B.: Lack of Increase in Antibody After Second Injection of Influenza Virus in Man, *Australian J. Exper. Biol. & M. Sc.* 22:301 (Dec.) 1944.

5. Salk, J. E.: Reactions to Concentrated Influenza Virus Vaccines, *J. Immunol.* 58:369 (April) 1948.

6. Bruyn, H. B.; Meiklejohn, G., and Brainerd, H. D.: Influenza Vaccination: A Comparison of Antibody Response Obtained by Various Methods of Administration, *J. Immunol.* 62:1 (May) 1949. Fazekas de St. Groth, S., and Donnelley, M.: Studies in Experimental Immunology of Influenza: The Protective Value of Active Immunization, *Australian J. Exper. Biol. & Med. Sc.* 28:61 (Jan.) 1950. Appleby, J. C.; Himmelweit, F., and Stuart-Harris, C. H.: Immunisation with Influenza Virus A Vaccines: Comparison of Intradermal and Subcutaneous Routes, *Lancet* 1:1384 (June 30) 1951.

7. Henle, W., and Henle, G.: Effect of Adjuvants on Vaccination of Human Beings Against Influenza, *Proc. Soc. Exper. Biol. & Med.* 59:179 (June) 1945. Friedewald, W. F.: Adjuvants in Immunization with Influenza Virus Vaccines, *J. Exper. Med.* 80:477 (Dec.) 1944. Salk.³

8. Fazekas de St. Groth, S., and Donnelley, M.: Studies in Experimental Immunology of Influenza: Enhancement of Immunity by Pathotopic Vaccination, *Australian J. Exper. Biol. & M. Sc.* 28:77 (Jan.) 1950.

9. Andrewes, C. H.: Prophylaxis of Virus Infections, with Special Reference to the Use of Vaccines, *Brit. M. J.* 2:1007 (Dec. 11) 1948.

between the administration of the B and A viruses is extended to a week or more, the development of type A infection is not prevented. The interference is thus effective for a very short time, presumably only while an active though inapparent infection with type B virus is in progress. Whether this procedure has practical application in man remains to be seen, but it is encouraging that many avenues of approach to this difficult problem are being explored. If current predictions are fulfilled, optimism may replace pessimism in this field.

ATHLETIC PROGRAMS IN INDUSTRY

When policy is established in industry, many opinions, experiences, and recommendations of various persons are used to delineate modes of action. The value of such combined operation has been evident in many segments of industry, but the procedure has not yet been applied with maximum effectiveness in the field of company-sponsored recreation. An organization interested in the worker's welfare may institute or permit a program of industrial health and a scheme of recreation that will include strenuous and mild exercise, both outdoor and indoor, and individual and team participation for male and female employees. Participation is encouraged by awarding trophies and reporting activities and names of participants in the sports columns of the local plant newspaper. The pleasures of such pursuits, however, may be overshadowed by the development of "baseball fingers," "tennis elbows," and "strawberries" on the base stealers' hips. Insults of nontraumatic origin, such as coronary thrombosis, also are a potential danger in the out-of-condition, overweight, middle-aged or older shipping clerk suddenly turned shortstop.

Uniforms, transportation, and equipment are furnished to the company's baseball and football players. Too rarely, however, is skilled medical advice sought by the recreation director, even though frequently he and the medical director occupy blocks on the same industrial relations division organizational chart.

Daily, industrial workers are exposing themselves to the dangers of after hour athletics without the necessary health clearance or the conditioning needed for arduous exertion. Middle-aged employees leading a sedentary life in a supervisor's chair decide to try to regain their prowess of 25 years ago on the gridiron or cinder track. Without physical retraining they throw sudden strains on cardiac musculature that for many years had to answer no such demands, or, with little knowledge of the game, these athletic dilettantes will catch baseballs on their extended finger tips, turn ankles during poorly executed slides, or twist knees.

A safety engineer once asked, "Why do we try to protect these fellows during the day, and then have them, at night, put themselves through a meat grinder?" Those who practice industrial medicine often have failed, perhaps through no fault of their own, to join with the athletic directors to assure that each participant is physically fit to undertake these activities, that he is familiar with the techniques of play, and that the sport presents no unusual hazards to him. A system that will provide medical clearance for all participants will obviate many of the

injuries and illnesses encountered among untrained evening-time athletes.

In a recent report of a foreign medical correspondent¹ training in physical exercise was defined as a "regular and systematic repetition of an activity which involves also the superior nervous functions. The factors which condition it are common to all persons; among the most important ones are the constitutional factor, the cardio-circulatory, the respiratory, the central nervous and sympathetic nervous systems, the endocrine, osteoarticular and muscular factor, and the factors of nutrition and metabolism." Where is the industrial worker given training on his return to the sandlot? Where is he assured that the condition of his organ systems enumerated above is such that participation in athletics will be safe?

Industry can care for its overambitious, overweight, and overage 7 p. m. athletes, by determining before the season begins that all applicants for the plant team can meet the rigors of competitive sport. Health supervision is not an eight-to-five o'clock concept—it can be extended to make industrial recreation enjoyable, safe, and invigorating, and not a fracture producing, sprain producing, or otherwise incapacitating experience.

PHYSICIAN POLL ON INTERN TRAINING

In a previous issue of THE JOURNAL, the Council on Medical Education and Hospitals announced the appointment of an Advisory Committee on Internships to study problems relating to intern training and to consider the entire question of the internship in its broadest aspects.¹ The announcement pointed out that the problems that have arisen as a result of the increasing disparity between the number of internships and the number of applicants emphasize the need for a reclarification and redefinition of the internship and its present place in medical education.

At its first meeting, the Advisory Committee decided to conduct a poll of the graduates of the classes of 1937 and 1947 to provide certain basic information in considering the internship as it has been conducted and in making recommendations for the future. Approximately 11,000 physicians will be included in the poll. These graduates are being asked to evaluate their own internship and to comment on intern training in general in the light of their experience as practicing physicians. The immediate response to the questionnaire has been excellent. The large number that were completed and sent back to the Council by return mail indicate the genuine interest in the efforts of the Council and its Advisory Committee to improve the quality of intern training. It is hoped that all members of these two classes will cooperate and assist the Committee with its study. The results of the poll will be most helpful to the Committee in evaluating trends in intern training during the 10 year period represented by these graduates and will enable them to base their recommendations on specific data not presently available. The results of the poll, as well as the study as a whole will be awaited with interest.

1. International Congress of Medical Aspects of Sport, correspondence (Italy), J. A. M. A. 144: 200 (Sept. 9) 1950.

1. Approved Residencies and Internships, J. A. M. A. 147: 384 (Sept. 29) 1951.

ORGANIZATION SECTION

FEDERAL MEDICAL LEGISLATION

Federal Scholarships

Representative Furcolo of Massachusetts introduced H. R. 6161 proposing to provide for loans to enable needy and scholastically qualified students to continue education after high school. This bill would establish, principally with federal money, a "federal scholarship fund" for college education. Beneficiaries would be needy and scholastically qualified persons nominated by officials of the several states who are acceptable to the U. S. Commissioner of Education. Scholarship loans would not exceed \$1,000 per year for four years of college studies and/or \$1,500 a year for the first four years of postgraduate studies after college. This bill was written to include students desiring to pursue any college course. Under its provisions, although medical students are not specifically named, certain needy and scholastically qualified premedical and medical students could qualify for loans. Loans would be repaid by periodic payments, beginning the second year after completion of study, in 10 equal payments plus interest. Loans would not be made until the student had been accepted by an educational institution. A provision in the bill prohibits federal employees from supervising, controlling, or regulating personnel or curriculum of educational institutions that accept loan students.

Social Security Amendment

H. R. 6213 was introduced by Representative Burnside of West Virginia and would amend the Social Security Act to provide disability insurance benefits for totally disabled persons. It provides that the administrator of the Federal Security Agency shall make regulations for determinations of disability and redeterminations. It would be permissible for a physician, not an employee of the United States, to be designated to make examinations and to be paid therefor. Beneficiaries who refuse to be examined without good cause and refuse to accept rehabilitation services could be denied benefits. The administrator would be authorized to enter into voluntary working arrangements with private physicians, dentists, hospitals, and other persons, groups, and agencies providing medical care and hospitalization for examination and rehabilitation of beneficiaries. A totally disabled person is defined as one unable to engage in any substantially gainful activity by reason of any medically demonstrable physical or mental impairment, including blindness. This bill is similar to the proposal contained in H. R. 6000 of the 81st Congress, which was deleted from H. R. 6000 before it became law.

Federal Nursing Education

Representative Elliott of Alabama introduced H. R. 6185 to amend the Public Health Service Act to provide a program of grants and scholarships for education in the field of nursing. This bill is identical with H. R. 910 (Bolton). It would provide federal funds estimated at 47 million dollars annually for scholarships, for construction, and for increasing teaching equipment and personnel for nurse education. It provides varying amounts for scholarships from the practical nurse level through the baccalaureate degree. The Surgeon General of the Public Health Service would be authorized to use 5 million dollars annually to get construction under way, but no grant would be in excess of 50% of the cost of construction and equipment.

Medical Benefits to Coast Guard Personnel Dependents

H. R. 6212, introduced by Representative Bonner of North Carolina, would authorize and direct the Commandant of the United States Coast Guard to furnish hospitalization and medical, surgical, and dental care and treatment for dependents of personnel of the United States Coast Guard under such regulation as he may prescribe.

Federal Assistance to Blind and Handicapped

Representative Celler of New York introduced H. R. 6215, proposing to assure the provision of all necessary services to rehabilitate disabled persons for and to establish them in remunerative employment, to make special provision for the blind and other severely disabled persons. This bill is identical with S. 1202, previously reported.

STATE MEDICAL LEGISLATION

Arizona

Bills Introduced.—H. 10, proposes the creation of a board of physical therapy examiners and defines physical therapy as the treatment of a bodily or mental condition by the use of the physical, chemical, or other properties of heat, light, water, or electricity, or by massage and active and passive exercise, prescribed by a licensed physician, but does not include the use of roentgen rays and radium for diagnostic and therapeutic purposes or the use of electricity for surgical purposes, including cauterization. H. 22, to amend the medical practice act, proposes to authorize the board of medical examiners to revoke or suspend a certificate to practice medicine of any person who is physically or mentally unable safely to engage in the practice of medicine and surgery or when the holder of a certificate has been declared insane. H. 27, proposes an appropriation for setting up and maintaining, in cooperation with the federal government, a statewide preventive mental health program. H. 100, proposes the creation of a board of certified practical nurse registration for the purpose of examining and licensing persons desiring to engage in practical nursing. H. 133, proposes the creation of a board of examiners of sanitarians to license and examine persons trained in sanitary science and technology qualified to carry out educational and inspectional duties and enforce laws in the field of sanitation. H. 146, to amend the basic science act, proposes to exempt chiropractors from the operation of its provisions. S. 5, proposes to exempt optometrists from jury duty. S. 25 proposes the enactment of a uniform narcotic drug act.

Colorado

Bills Introduced.—SJR. 9, proposes the creation of a special committee to conduct a thorough study of the laws of the state concerning narcotic, hypnotic, and dangerous drugs, and the methods of enforcement thereof. SJR. 12, proposes the creation of a legislative committee to make a thorough study and investigation with respect to the needy aged of the state and particularly with reference to overcrowded conditions in state county, and public hospitals and in private hospitals and sanitariums.

Georgia

Bills Introduced.—H. 609, proposes to authorize the board of examiner for nurses to examine and license applicants desiring to practice as practical nurses. H. 821, proposes the creation of liens in favor of hospital upon rights of actions, suits, claims, counterclaims, or demands of person in the hospital for the amount of reasonable charges of the hospital for treatment and care of such persons. H. 875, proposes to amend the premarital examination law so as to permit the necessary certificates to be signed by osteopaths. H. 928, proposes to amend the sales tax so as to exempt the sales of medicines. H. 931, proposes the creation of a Georgia Board of Massage to examine and license persons desiring to practice massage which is defined as the art of body massage either by hand or with any mechanical or electrical apparatus for the purpose of body massage, reducing or contouring, the use of oil rubs, salt glows, hot and cold packs, tub, shower, sitz and similar baths. S. 313, proposes to authorize the board of health to make use of the injunctive process in enforcing its rules and regulations.

Kentucky

Bills Introduced.—H. 114, to amend the workmen's compensation act proposes that medical testimony in workmen's compensation cases shall be limited to not more than two physicians for each party. H. 137 proposes a new medical practice act which would be applicable to physicians and osteopaths. S. 35, proposes the creation of an alcoholic rehabilitation commission to establish and equip a clinic for the diagnosis, classification, confinement, treatment, and study of chronic alcoholics. S. 50, proposes the enactment of a hospital licensing law. S. 100, proposes to authorize the alcoholic study commission to make a comprehensive study on the problem of alcoholism, the existing methods and facilities for treatment, of the present program for public education on alcoholism and the present status of the laws of the state in regard to alcoholism.

Massachusetts

Bills Introduced.—H. 1283, proposes regulations for making impounded animals available for humane, scientific teaching and research. The licensing features of the law would be under the supervision of the state board of registration of veterinary medicine. H. 1349, proposes that every cit

with a population of more than 100,000 and having a municipal hospital shall provide ambulance services to and from said hospital in an ambulance owned and operated by the city, available for use 24 hours a day and staffed by a male nurse and driver. H. 1466, proposes the establishment of a new medical school by the University of Massachusetts. H. 1469, proposes the creation of a new medical school to be known as the University of Massachusetts Medical School. H. 1892, proposes the creation of a special commission to make a study relative to the care, treatment and rehabilitation of sexual psychopaths. H. 1894, proposes to direct the committee on public welfare to make a survey relative to the number of persons confined in hospitals under the control of the department of mental health who should be transferred to other types of hospitals or rest homes or released to their families. S. 349, to amend the medical practice act relating to reciprocal registration of physicians, proposes that no person shall be registered without examination if he is a graduate of a medical school located outside of the United States or its territorial limits. S. 400, proposes the creation of a committee to make an investigation and study of the department of mental health and institutions under control of this department.

Michigan

Bills Introduced.—H. 41, proposes that all school bus drivers must annually produce a certificate of a reputable physician certifying to his physical fitness and mental alertness to drive a bus. H. 165, proposes to authorize the department of welfare to enforce its regulations by means of the *Injunctive process*. H. 183, to amend the chiropractic act, proposes that the license provided for in this act shall entitle the holder thereof to practice medicine in the state of Michigan and for the purpose of the act provides that chiropractic is based on the premise that the nerve system coordinates all systems and all physiological functions of the human body; that interference with the nerve control of the systems impairs their functions and induces disease by rendering the body less resistant to infection or to other exciting causes. Under the proposal a person practices chiropractic when in the course of such practice he diagnoses and/or when he corrects or attempts to correct human ailments by the adjustment of the spinal column and other health measures common to the healing arts, and the procedure preparatory thereto, provided he shall not use drug treatment, surgery where tissues are cut or severed or midwifery. SCR. 11, proposes the creation of a special committee to continue to study the problems pertaining to narcotics and to report their findings to the 1953 session of the legislature. S. 26, proposes to abolish the office of coroner and create a medical examiner system within the state. S. 64, proposes certain amendments to the law regulating and licensing optometrists. S. 65, proposes that any person who shall employ another person in migratory or seasonal agricultural labor shall be guilty of a misdemeanor unless the person so employed shall carry or furnish a certificate from a physician licensed in the state certifying that the person is not afflicted with tuberculosis. S. 69, proposes the creation of a state department of health and outlines the duties of such department. S. 85, relating to autopsies, proposes that whenever an autopsy is performed upon the body of a person when intoxication may have been the direct or indirect cause of death, or a contributory factor thereto, a blood sample shall be taken to determine the degree of alcohol in the blood of the deceased. S. 92, to amend the law relating to narcotics, proposes to make certain penalties, applicable just to minors, applicable to all persons who violate the act. S. 144, proposes to restrict the sale of narcotic drugs to persons licensed so to do. The term narcotic is defined to include cocaine, opium, morphine, codeine, heroin, barbituric acid, chloral hydrate, and all parts of the plant cannabis sativa. S. 188, to amend the workmen's compensation act, proposes to require employers to furnish dental services when needed.

Mississippi

Bills Introduced.—S. 38, proposes the creation by the attorney general of a state bureau of investigation to have charge of and administer the agencies and activities which are set up for the identity of criminals, for their apprehension, for the systematic analysis of evidence of crime and investigation and preparation of evidence to be used in criminal courts. S. 84, proposes the creation of a Mississippi State Board of Examiners of Practical Nurses to examine and license persons desiring to practice as practical nurses. S. 101, proposes to require both applicants for a marriage license to furnish a certificate executed by a physician licensed to practice in Mississippi or licensed to practice in any or all of the other states of the Union, certifying freedom from syphilis. S. 122, proposes the creation of a Mississippi Bureau of Investigation which would have within it a division of scientific detection and identification.

New Jersey

Bills Introduced.—A. 133 and A. 175 propose amendments to the temporary disability benefits law. A. 174, proposes to authorize certain veterans with unusual qualifications to be examined by the state board of medical examiners. Such veterans must be more than 40 years of age, of good moral character, a citizen of the United States and a resident of New Jersey, a graduate of a four year course of study in high school, a graduate of a two year premedical course in premedical college, graduate of a four year college with the degree of Doctor of Medicine, at least one year experience as an intern, at least 10 years directing a clinical laboratory, is a licensed pharmacist and who shall have practiced pharmacy for five years, at least two years experience as an assistant in an x-ray laboratory and has passed an examination given by a state board in another state on the subjects of anatomy, physiology, pathology, chemistry, and bacteriology. A. 179, to amend the law relating to examination of hospital records, proposes that the custodian of any hospital records shall permit examination of such record in connection with any claim for compensation or damages for personal injury or death

resulting therefrom by any person authorized by any other law to make such examination. A. 206, proposes that a person duly authorized to practice medicine, surgery or dentistry or a registered nurse shall not be allowed or compelled to disclose in court or to any public officer any confidential communication or any information which he acquired in attending a patient in a professional capacity and which was necessary to enable him to act in that capacity, without the consent of the patient. SJR. 3, proposes the creation of a commission to investigate the reasonableness of the rates now being assessed, allowances being paid to hospitals for services rendered to policy holders, as well as the salaries, fees, and expenses being paid to their executive and attorneys and also the formation by them as a nonprofit organization of a holding company to purchase real estate. S. 24, proposes to authorize the creation of a debt of the state in the amount of 25 million dollars for the construction and maintenance of a state college of medicine, dentistry and veterinary medicine. S. 35 and S. 36 propose amendments to the temporary disability benefits law. S. 38, proposes to prohibit a deduction from wages to defray the costs of medical examinations of employees and prospective employees.

New York

Bills Introduced.—A.R. 32, proposes to memorialize the United States to establish a United Nations agency as the sole legal channel for international trade in opium. A. 631 and A. 637, to amend the penal law, propose to prohibit the sale of hypodermic needles without a written prescription of a duly licensed physician, unless the sale is to a physician, dentist, a hospital, or the like. A. 686, to amend the education law relating to the use of the x-ray, proposes to permit physiotherapists to use the roentgen ray or x-ray providing they have had a course of not less than two years in radiography technique at a college or university approved by the state education department. A. 727, to amend the state income tax law, would permit taxpayers to deduct all medical expenses exceeding 5% of the net income of the taxpayer. A. 863 and S. 717, propose regulations authorizing the state commissioner of health to license and designate approved laboratories and institutions which conduct scientific tests or experiments on living animals. A. 868 and S. 784, to amend the workmen's compensation act, propose to authorize the board upon application made by an employee, employer or carrier, to cause an examination of an injured employee by a physician designated by the commission especially qualified with respect to the diagnosis or treatment of the disability for which compensation is claimed. A. 880, to amend the penal code, proposes that authorization for an autopsy may be given by an adult, child, parent, brother, or sister of the deceased if there is no surviving husband or wife. A. 970, proposes to require applicants for an operators or chauffeurs license to present a certificate signed by a duly licensed physician or optometrist attesting that the applicant has been examined as to his eye sight and found competent to operate a motor vehicle. A. 1028, to amend the mental hygiene law relating to the certification of qualified psychiatrists, proposes to require three, rather than two, years' full time experience in order for a person to be so certified. S. 628, proposes the creation of a temporary commission to undertake and complete a thorough study of the feasibility of requiring each resident of the state to take an annual health examination. S. 678, proposes to define the words "narcotic drugs" so as to include "dromoran" and "dromoran" hydrobromide.

South Carolina

Bills Introduced.—H. 1712, proposes to exempt the gross proceeds of sales of medicine prescribed by a licensed physician from the sales tax law. H. 1760, proposes the creation of a state board of examiners of physical therapy for examining and licensing persons desiring to practice physical therapy which is defined to mean the treatment of any bodily or mental condition of any person by the use of the physical, chemical, and other properties of heat, light, water or electricity, massage, and active and passive exercise. The roentgen rays and radium for diagnostic purposes and the use of electricity for surgical purposes, including cauterization, would not be authorized by this proposal. H. 1775, proposes regulations for the detention, guardianship, care, and treatment of mentally ill and mentally deficient persons.

Virginia

Bills Introduced.—H. 11 and S1, propose to amend the narcotics law in connection with the penalties for violation thereof, especially when the violation involves the sale of narcotics to a minor. H. 362, proposes that no drug, preparation or appliance having a special utility for the prevention of venereal disease shall be sold except by duly licensed practitioners of medicine or in pharmacies and retail stores having a permit from the state board of pharmacy. The offering for sale, distribution, or other disposition of such goods by means of a vending machine is prohibited. H. 137, to amend the uniform narcotic act, proposes special penalties for dispensing narcotics to minors. H. 225, proposes regulations for the granting of annual nursing scholarships.

MEDICAL ECONOMICS

The Bureau of Medical Economic Research recently published M-55, "Subject Index to Bulletins and Miscellaneous Publications of the Bureau of Medical Economic Research, 1947-1951." A copy may be obtained by writing to the Bureau of Medical Economic Research, American Medical Association, 535 N. Dearborn St., Chicago.

MEDICAL NEWS

CALIFORNIA

Course on Physics in Radiology.—The University of Southern California Division of Medical Extension Education is presenting a course, Essential Physics in Radiology, from March 10 to May 26 covering x-ray, radium, and isotope radiation, and clinical applications of isotopes. The course will be offered every Monday from 8 to 10 p. m.; the first six weeks' lectures will be presented at Los Angeles County Hospital and the last six at the Cedars of Lebanon Hospital. The fee is \$50. Information may be obtained from the University of Southern California School of Medicine, Division of Medical Extension Education, 1200 N. State St., Los Angeles 33.

Advances in Public Health.—The acting state health director, Dr. Malcolm H. Merrill, has cited the following among other advances in public health in 1951: Completed building projects provided 2,160 new hospital beds, and construction started will provide an additional 4,000 beds. Most of the construction was financed by private funds, but federal and state funds were granted to 11 projects. However, the increase in population has outstripped construction so that the hospital bed shortage is still acute. In 1951 state health department personnel were loaned to the Office of Civil Defense to plan the services that would be needed in California in a disaster. A permanent Division of Medical and Health Services was then set up in San Francisco to operate under joint direction of the state directors of public health and civil defense. Area organizations of doctors, nurses, hospitals, public health technicians, and similar personnel were developed in 10 "Civil Defense Regions" of California. The year's planning includes the requisitioning of medical supplies for 683 first-aid stations and the completion of special manuals for program administration, utilization of local resources, operation of first aid stations and hospitals, and emergency treatment of casualties.

DISTRICT OF COLUMBIA

Eleventh Davidson Lecture.—Dr. Jonathan M. Williams has been selected to deliver the 11th Davidson Lecture of the Medical Society of the District of Columbia, Feb. 20, in connection with the midwinter seminar. The title of the address will be "mygdaloid Nucleus." Dr. Williams is an associate in neurosurgery at George Washington University School of Medicine. The Davidson Lecture was established in 1929 to commemorate services rendered to the profession by Dr. Edward Young Davidson.

GEORGIA

Health Council Organized.—The Better Health Council of Georgia has been organized as an outgrowth of the Georgia Citizens Council, which was supported by the state. When state funds were withdrawn, the coordinating health agencies banded together to form the council. It is supported by the Medical Association of Georgia, the Medical College of Georgia, Emory University School of Medicine, Georgia Dental Association, Emory University School of Dentistry, Georgia State Nurses Association, State Department of Public Health, and private health agencies. Its purpose is to promote better health in Georgia, to organize regional health conferences and local health councils, and to promote coordination of various health agencies and interchange of information among these agencies. It has headquarters at 11 Pryor St., S. W., Atlanta 3. The executive secretary is Mrs. William Reid.

ILLINOIS

State Examinations for Physicians.—The Illinois Civil Service Commission, 501 Armory Building, Springfield, will conduct examinations for the following three positions at state institutions. Final date for applications is April 30. Positions are

open for Physician I, salary \$360 to \$550 per month, who can provide professional medical services in the general care and treatment of patients in state hospitals, clinics, and schools. He makes diagnoses and treats mentally and physically ill persons, and acts as supervisor to nursing personnel. Examinations will be held for Psychiatrist I, salary \$440 to \$660, who, under supervision, provides for the physical, neurological, and psychiatric care, study, and treatment of patients in state institutions, and for juvenile patients in child guidance institutes or outpatient clinics. It is desirable that the applicant have had two years of full-time experience in the practice of psychiatry at an approved hospital, clinic, institute, dispensary, or laboratory. For physicians at a child guidance institute, experience should include one year in the practice of juvenile psychiatry. The state is also seeking Tuberculosis Control Physicians I, with a salary of from \$440 to \$660, to perform specialized professional medical work in the examination, diagnosis, and treatment of tuberculosis patients in state institutions. The work may involve educational and consultative programs with professional and lay groups. One year of residency in an acceptable tuberculosis sanatorium or one year postgraduate training plus one year of experience in tuberculosis diagnosis, treatment, and control are the desirable qualifications.

Chicago

Personals.—Dr. Raymond G. Mann has joined the medical consultant staff of Armour Laboratories as regional medical director of the Midwest division. Dr. Cornelius J. O'Donovan, formerly chief of the medical service of the U. S. Public Health Service Hospital, San Juan, Puerto Rico, has been named assistant medical director in the clinical investigation service.

Society News.—The Chicago Society of Physical Medicine and Rehabilitation at their meeting Feb. 27 in the City of Chicago Welfare Convalescent Home will hear a discussion of the "City of Chicago Welfare Physical Medicine and Rehabilitation Program." The speaker will be Dr. Arthur A. Rodriguez, and the discussers, Dr. Frances Hellebrandt and Dr. Charles O. Molander. Physicians, other professional personnel, and their guests are welcome.

Tuberculosis X-Ray Service.—The Municipal Tuberculosis Sanitarium and the Tuberculosis Institute of Chicago and Cook County will conduct a free chest x-ray service in 1952. This year's program is the most ambitious yet undertaken in Chicago and is made possible by the increasing returns from the annual Christmas Seal sale. The death total in Chicago from tuberculosis last year dropped to 1,447 as compared to 1,798 in 1946, the year before the institute and the sanitarium merged their programs.

Annual Chicago Clinical Conference.—The 1952 clinical conference of the Chicago Medical Society will be held March 4-7 at the Palmer House. Speakers include:

- John R. Paul, New Haven, Conn., Poliomyelitis.
- Stanley P. Reimann, Philadelphia, General Care of the Cancer Patient.
- Mitchell I. Rubin, Buffalo, Fluid Balance in Diseases of Childhood.
- Richard H. Sweet, Boston, Diagnosis and Treatment of Benign Lesions of the Esophagus.
- George W. N. Eggers, Galveston, Texas, Fractures of the Ankle Joint.
- James J. Waring, Denver, Present Day Treatment of Pulmonary Tuberculosis.
- Richard G. Scobee, St. Louis, The Physician and the Cross-Eyed Child.
- Francis C. Grant, Philadelphia, Relief of Intractable Pain in Inoperable Cancer.
- J. Albert Key and Lee T. Ford, St. Louis, Management of the Patient with a Ruptured Disc.
- Albert Dorfman, Chicago, Rheumatic Fever.
- Rubin H. Flocks, Iowa City, Treatment of Benign Hypertrophy of the Prostate.
- Francis M. Rackemann, Boston, Advances in Treatment of the Allergic Diseases.
- Howard B. Sprague, Brookline, Mass., Diagnostic Problems in Cardiac Disease.
- Edward B. D. Neuhauser, Boston, Problems of Pulmonary Disease in Childhood.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

Leland S. McKittrick, Boston, Carcinoma of the Colon.
 Howard P. House, Los Angeles, Modern Management of Deafness.
 Ira H. Lockwood, Kansas City, Mo., Low Back Pain from the Viewpoint of the Radiologist.
 Armand J. Quick, Milwaukee, Newer Knowledge Concerning Hemophilia.
 Francis J. Braceland, Hartford, Conn., Psychiatric Aspects of Cortisone Administration.
 Richard D. Bryant, Cincinnati, Etiology and Treatment of Prolonged Labor.
 Wesley W. Spink, Minneapolis, Recognition and Management of Human Brucellosis.
 Max M. Strumia, Philadelphia, Practical Approach to Diagnosis and Therapy of Hemolytic Anemias.
 John W. Cline, President of the American Medical Association, San Francisco, Common Lesions of the Breast.
 Frank Glenn, New York, Stones in the Common Duct.
 Edgar Burns, New Orleans, Urologic Problems in Children.
 James S. Simmons, Boston, Community Health: Medicine's Contribution to National Security.
 Norman F. Miller, Ann Arbor, Mich., Postpartum Care.
 Edward C. Reifstein Jr., Oklahoma City, Effect of Steroids on Bone Disease of Aging People.
 Russell J. Blattner, Houston, Texas, Advances in Treatment of Viral and Rickettsial Diseases.

There will be roundtable luncheon discussions and panel discussions at the close of the Wednesday, Thursday, and Friday programs on "What's New in Medicine and Surgery," "Hematology," and "Obstetrics and Gynecology," respectively. The registration fee is \$5.

INDIANA

Medical Science Building.—Plans are underway for the construction of the Medical Science Building of the Indiana University Medical Center in Indianapolis. A 12-member committee is meeting at regular intervals to outline the plans. The building will relieve congested classroom and laboratory facilities of the dental and medical schools on this campus.

LOUISIANA

Annual New Orleans Medical Assembly.—The annual meeting of the New Orleans Medical Assembly will be held March 10-13 at the Municipal Auditorium in New Orleans. Guest speakers and the first of their three to four papers to be presented at the assembly include:

J. Arnold Bargen, Rochester, Minn., Diverticulitis of the Large Intestine: Its Importance in the Productive Years.
 Leroy A. Calkins, Kansas City, Kan., Prolonged Labor.
 Richard B. Cattell, Boston, Diverticula of the Gastrointestinal Tract.
 Edward L. Compere, Chicago, Neck, Shoulder, and Arm Syndrome.
 Claude F. Dixon, Rochester, Minn., Rectal Cancer: Its Management.
 Charles A. Doan, Columbus, Ohio, Leukemic States—Their Differential Diagnosis as a Basis for Selective Therapy.
 Jacob E. Finesinger, Baltimore, The Doctor-Patient Relationship.
 Frank C. Hamm, Brooklyn, Recent Developments in the Diagnosis of Renal Tumors.
 Leo V. Hand, Boston, Spinal Headache: Suggestive Causative Factors and Recommendations for Prevention and Treatment.
 John H. Lamb, Oklahoma City, Eczema.
 Hayes Martin, New York, Diagnostic Significance of a "Lump in the Neck."
 John P. Merrill, Boston, Use of the Artificial Kidney.
 Margaret M. Nicholson, Washington, D. C., Recent Trends in Immunization.
 William Parson, Charlottesville, Va., Appraisal of the Present Status of Cortisone and ACTH.
 Ralph A. Reis, Chicago, Functioning Tumors of the Ovary.
 Harold G. Scheie, Philadelphia, Retinal Changes Associated with Hypertension and Arteriosclerosis.
 John R. Schenken, Omaha, Primary Thrombocytopenic Purpura.
 Paul C. Swenson, Philadelphia, Problem of Early Diagnosis of Gastrointestinal Cancer.

Roundtable luncheons are scheduled for specialty groups on Tuesday and Thursday and for medicine and surgery on Wednesday. The speakers will address the luncheon gatherings. Color television of surgical operations and medical clinics originating in Charity Hospital will be transmitted to the Municipal Auditorium under the sponsorship of Smith, Kline, and French Laboratories. The registration fee of \$20 includes the round table discussions. A postclinical tour of Mexico will extend from March 15-29. The trip includes lectures and visits to hospitals as well as an extensive program of sightseeing. Physicians who wish to join the tour should address Mrs. Irma B. Sherwood, Executive Secretary, Room 103, 1430 Tulane Ave, New Orleans 12.

MASSACHUSETTS

Chemical Specificity in Biological Interactions.—Seminars on this subject are being presented at Harvard University during February and March. Their purpose is to assess the knowledge in a field that is important in understanding the chemical nature of interactions of enzymes and metals and of lipoproteins and steroid hormones presumed to be characteristic of bodily processes. The eight meetings, all on Thursdays except the last on Friday, March 28, are being held at 4:30 p. m. in Harvard Hall under the auspices of the Harvard University Laboratory of Physical Chemistry Related to Medicine and Public Health. The remaining seminar speakers are as follows:

Feb. 21, Jack Schubert, Ph.D., Chicago, Metal Organic Complexes and Their Relations to Metal-Protein Specificity.
 March 6, Carl F. Cori, St. Louis, Enzymatic Synthesis of Polysaccharides.
 March 13, Thomas F. Gallagher, Ph.D., New York, and Richard B. Turner, Ph.D., Houston, Texas, Studies on the Structure, Properties and Reactivity of Steroids.
 March 20, Vincent du Vigneaud, Ph.D., New York, Studies on the Hormones of the Posterior Pituitary.
 March 27, Waldo E. Cohn, Ph.D., Oak Ridge, Tenn., Influence of Ion Exchange Chromatography upon Our Concept of the Structure of Nucleic Acid.
 March 28, Shields Warren, Boston, Effects of X-Ray and Other Radiation on Proteins and Living Tissues.

MICHIGAN

Michigan Clinical Institute.—This institute will be held at the Sheraton-Cadillac Hotel, Detroit, March 12-14. The program will emphasize diagnosis and treatment. Forty lecturers and clinicians will appear on the program, which has been divided among the subjects surgery, obstetrics and pediatrics, medicine, adult health, heart, and metabolic diseases. Out-of-state speakers are as follows:

Truman G. Blocker Jr., Galveston, Texas, Treatment of Burns.
 Edward J. McCormick, Toledo, Ohio, Surgery of Traumatism.
 Oscar Swineford Jr., Charlottesville, Va., Hay Fever and Asthma.
 Garfield G. Duncan, Philadelphia, Management of Diabetes.
 Jay A. Myers, Minneapolis, Diagnosis of Early Tuberculosis.
 Charles F. Wilkinson Jr., New York, Arteriosclerosis.
 Raymond O. Muehrer, St. Louis, Differential Diagnosis of Jaundice.
 Richard H. Freyberg, New York, Arthritis.
 Franklin M. Hanger, New York, Cirrhosis of the Liver.

The following speakers will address those attending the subscription luncheons:

March 12, Howard A. Rusk, New York, Dynamic Therapeutics in Chronic Disease.
 March 13, Lauren V. Ackerman, St. Louis, R. S. Sykes Lecture, Benign and Borderline Epithelial Tumors of Large Bowel.
 March 14, Samuel A. Levine, Boston, Importance of History and Physical Examination in Diagnosis of Heart Disease.

Dr. Norvin Keifer, Washington, D. C., director of health and special weapons defense division of the Federal Civil Defense Administration, will speak on "The Physician in Civil Defense" March 12 at 8:30 p. m. at the annual civil defense meeting to be held during the institute. The civil defense meeting is co-sponsored by the Wayne County Medical Society, Michigan Clinical Institute, and the Michigan State Medical Society.

MONTANA

State Association Interim Session.—This session of the Montana Medical Association will be held at the Placer Hotel in Helena Feb. 29 through March 1. The scientific program will be held on Saturday. The guest speaker at the banquet Feb. 29 will be Dr. R. B. Robins of Camden, Ark., who will speak on "Medicine and This Changing World."

NEW JERSEY

Course in Diseases of the Chest.—The New Jersey Chapter of the American College of Chest Physicians and the New Jersey Academy of General Practice are sponsoring postgraduate lectures on four consecutive Wednesdays at 1:30 p. m. beginning Feb. 20 at the Essex House on Broad Street in Newark. A review of the latest procedures used in the diagnosis and treatment of chest diseases will be presented by physicians, most of whom are from New York and Philadelphia. A fee of \$25 must accompany registration. Interns and residents will be accepted at a fee of \$10. Checks should be made payable to the college and sent to Dr. J. R. Herradora, 2750 Blvd., Jersey City, N. J.

State Heart Association Meeting.—The New Jersey Heart Association will hold a scientific session March 19 at the Academy of Medicine in Newark, beginning at 2 p. m. Papers will be presented by the following out-of-state speakers:

- J. Russell Elkinton, Philadelphia, Sodium and Potassium Metabolism in Cardiacs.
- Charles L. Burstein, New York; The Heart During Anesthesia.
- Harry Mandelbaum, New York, Ballistocardiography in Medical Practice.
- Dwight E. Harken, Boston, Surgery of Cardiac Disease.
- Leo M. Taran, New York, Modern Diagnosis and Treatment of Rheumatic Fever and Its Complications.
- Stewart Wolf, New York, Circulatory Responses to Life Situations.

NEW YORK

Hospital News.—The new three story million dollar wing of the Terrace Heights Hospital, Hollis, which was dedicated January 13, is equipped to care for 70 patients and increases the hospital's bed capacity to 109.

Personal.—Dr. Stiles D. Ezell of Middletown has been appointed secretary of the state board of medical examiners, effective Feb. 15, succeeding Dr. Jacob L. Lochner Jr. of Albany, who has become assistant medical director of the state workmen's compensation board.

New York City

Society News.—Drs. George Stein and L. Hyman Gold of Montefiore Hospital will present a paper entitled "Oral Lesions in Nutritional Deficiencies: An Experimental and Clinical Study" at the monthly conference of the New York Institute of Clinical Oral Pathology Feb. 25 at the New York Academy of Medicine, Room 440, at 9 p. m.

Separate Department of Anesthesiology at Columbia.—Dr. Emanuel M. Papper, professor of anesthesiology, has been appointed head of the newly formed department of anesthesiology at Columbia University College of Physicians and Surgeons. The study and teaching of anesthesiology previously had been conducted under the direction of the department of surgery. With a faculty of 13 the department will expand its research facilities.

Course in Radiologic Physics.—The 20th course in the field of atomic physics will be offered by Columbia University in the coming session. The course will be given in the School of General Studies by Edith H. Quimby, associate professor of radiology, and Carl Braestrup, associate in radiology, who is director of the Physics Laboratory for the New York City Department of Hospitals. The course is designed to meet the needs of non-medical personnel in industry and research who are using various forms of radiation in their every-day work. After a survey of the basic physical facts and theory of radiation, the course treats of such topics as radiation measurement, dosage problems in the use of x-rays and radium, protection against radiation, radiobiology, and the use of radioactive isotopes.

Fetal Salvage Clinic.—A preconception fetal salvage clinic, the first in the metropolitan New York area, has been opened at the Beth-El Hospital, Brooklyn. The aim of the clinic is to help couples who have a history of miscarriage, premature births, stillbirths, or a congenitally defective infant. In addition to a physical examination including an endocrine study, blood chemistry and serological studies, urinalysis, biopsy, and semen analysis, there will be interviews by psychiatrists, nutritionists, and social workers. Twenty-five physicians are assigned to work in the clinic. The first patients being tested are from the hospital's prenatal clinic or have been accepted from referrals of private physicians. A similar clinic, which is reported to be the first in the country, was started recently at the State University of New York College of Medicine at Syracuse.

PENNSYLVANIA

Hospital News.—Construction of two new wings of the Memorial Hospital of Monongahela was scheduled to begin in January. The additions, to cost about \$900,000, will expand the present facility of 100 beds to 140.

Philadelphia

Virus Laboratory.—The Langbord Virus Laboratory is now being established at the Hahnemann Medical College and Hospital of Philadelphia under the direction and supervision of Amedeo Bondi, Ph.D., head of the department of bacteriology. The laboratory is made possible through an initial gift of \$10,000 to the college by friends of Dr. Joseph Langbord, medical director of the Sidney Hillman Center of Philadelphia.

Dr. Dixon Becomes Health Commissioner.—Dr. James P. Dixon, manager of the department of health and hospitals, Denver, became commissioner of health Jan. 7, succeeding Dr. Rufus S. Reeves, who has been director of public health since 1944. The title of director of public health was changed under the new city charter which became effective in January. Dr. Dixon was director of the municipal hospital in Denver and had been director of the city's combined department of health and hospitals. He was also an assistant professor in the department of preventive medicine and public health at the University of Colorado School of Medicine.

Grant to Aid New Teaching Program.—To implement a new "doctor-in-training" program instituted at the University of Pennsylvania, the Commonwealth Fund of New York has awarded a grant of \$22,500 annually for two years. Under the new program students in the first year of their medical education are assigned to individual families in the Philadelphia area, whom they serve until their graduation as family health advisors with close faculty supervision. The grant to the university is made in favor of the department of public health and preventive medicine, of which Dr. John P. Hubbard is chairman. The Commonwealth Fund allotments are earmarked specifically for support of the "doctor-in-training" phase of the public health program at the university.

TENNESSEE

Appointed Professor of Surgery at Vanderbilt.—Dr. Henry W. Scott Jr., associate professor of surgery, Johns Hopkins Hospital, Baltimore, has been appointed professor of surgery at Vanderbilt University School of Medicine and surgeon-in-chief to the Vanderbilt University Hospital, succeeding Dr. Barney Brooks, who will become professor emeritus. Dr. Scott was appointed instructor in surgery at Johns Hopkins School of Medicine in 1946, was promoted to assistant professor of surgery in 1948, and to associate professor in 1950. Dr. Brooks came to Vanderbilt University School of Medicine 25 years ago.

TEXAS

Visiting Lecturer.—Ludwig von Bertalanffy, Ph.D., of the department of biology of the University of Ottawa, Canada, as guest speaker at the University of Texas School of Medicine, Galveston, March 10-12, will discuss three subjects, "Quantitative Laws in Metabolism, Growth, and Morphogenesis," "The System Concept in Biology," and "Dynamic Models in Psychology."

Fort Worth Heart Program.—In 26 months of operation the Fort Worth Heart Association's mobile health unit has checked 15,111 persons in 183 local business establishments for heart disease. Of the total surveyed, 1,180 were either suspected of having heart disease or were classified as borderline cases. The mobile unit is being used to create a public consciousness of heart disease, thus bringing about direct treatment of many cases that otherwise might go untreated. In conjunction with the services, the association sponsors a free cardiac clinic and weekly cardiac conferences. Persons with suspected heart disease uncovered by the survey team who cannot afford private treatment and who are otherwise eligible for City-County Hospital aid are referred to the clinic for further diagnosis and prolonged treatment. More than 200 persons are presently being treated. Volunteers from the Fort Worth Club of Internists staff the clinic on a rotating quarterly basis, four to six serving at a time. Private physicians and the cardiac clinic staff submit cases to the cardiac conference held each Thursday for diagnosis and suggested treatment. This method makes possible a valuable teaching tool for the doctors, and also serves as a check on the diagnosis made by any one physician. The conference is a required part of the training of interns and the resident staff of the City-County Hospital.

WASHINGTON

University Appointments.—Dr. George G. Sutherland has been appointed clinical associate professor in psychiatry at the University of Washington School of Medicine, Seattle. Frank M. Huennkens Jr., Ph.D., has been made assistant professor in the department of biochemistry.

Society News.—Dr. Clark C. Goss became president of the King County Medical Society for 1952 and Dr. Merrill Shaw was voted president-elect at the election January 7. Dr. Frederick A. Tucker was elected to a second term as secretary-treasurer. All three are residents of Seattle.

WEST VIRGINIA

Society News.—Dr. William P. Warden of Charles Town has been elected president of the Eastern Panhandle Medical Society to serve during 1952. Dr. George O. Martin of Martinsburg was reelected secretary-treasurer.

Future Nurse Club.—A "Future Nurse Club," the first in West Virginia, has been organized at Harrisville High School as the result of work by the Woman's Auxiliary to the Harrison County Medical Society. The organization of the new club followed the suggestion by Mrs. John F. McCuskey of Clarksburg, president of the state auxiliary, that students interested in nursing band together and form clubs similar to future teacher, future homemaker, and future farmer clubs. The main purpose of the organization, which now has 22 members, is to help alleviate the acute shortage of nurses in this state, and it is part of the nurses recruitment program of the Harrison auxiliary. The girls visited each department of St. Mary's School of Nursing and the Union Protestant School of Nursing in Clarksburg. Several members of the state and Harrison County auxiliaries accompanied them.

WISCONSIN

Study of Susceptibility to Poliomyelitis.—An \$8,110 March of Dimes grant has been presented to the University of Wisconsin Medical School, Madison, for study of the effect of certain chemicals on susceptibility to experimental poliomyelitis. The funds will be used by Dr. Aaron F. Rasmussen, associate professor of medical microbiology and preventive medicine. He will collaborate with Paul F. Clark, Ph.D., and Conrad A. Elvehjem, Ph.D.

GENERAL

Society Elections.—Among the officers of the International Society of Angiology for 1951-1953 are Dr. Emile F. Holman, San Francisco, president, and Dr. Henry Haimovici, 105 East 90th St., New York 28, secretary-treasurer.

Research in Problems of Sex.—The Committee for Research in Problems of Sex of the National Research Council expects to have a few thousand dollars available for new grants-in-aid during the fiscal period July 1, 1952, to June 30, 1953. Applications will be received until March 15. Blanks may be obtained from the Division of Medical Sciences, National Research Council, 2101 Constitution Ave., Washington 25, D. C.

Orthopsychiatric Association Meeting.—The annual meeting of the American Orthopsychiatric Association will be held in the Chalfonte-Haddon Hall Hotels, Atlantic City, N. J., Feb. 25-27 under the presidency of Dr. James M. Cunningham, Detroit. The program has been divided into section meetings that will take up problems of diagnosis and therapy. There will be a series of case workshops and exhibits. The registration fee for nonmembers is \$4.

Foundation Prize for Cerebral Palsy Paper.—The Louis Leffkoe Memorial Foundation offers a prize of \$500 for the most worthwhile original contribution to the medical knowledge of cerebral palsy. The paper, which may cover any aspect of the subject, is to be submitted to the trustees of the foundation, 601 Medical Arts Building, 16th and Walnut Streets, Philadelphia 2, on or before September 1, 1952. The prize is open to anyone who can contribute to the medical knowledge of the subject.

Interurban Neurosurgical Society.—This society will meet at the University Club of Chicago Feb. 23 at 9 a. m. The program, which may be heard by invitation only, is as follows:

H. Russell Meyers, Iowa City, Experimental Studies in the Hyperkinetic Disorders.

Donald D. Matson, Boston, Treatment of Congenital Hydrocephalus.

Kermit Christensen, Ph.D., St. Louis, Sympathetic Nerve Supply of Cerebral Blood Vessels.

Max S. Sadove, Chicago, Anesthesia in Neurosurgery.

Pan-American Ophthalmologic Congress.—At the congress of the Pan-American Ophthalmological Association in Mexico City in January a gold medal was presented to Dr. Alberto Vazquez Barriere of Uruguay for his contributions to ophthalmology. Mrs. Audrey Hayden Gradle, widow of Dr. Harry S. Gradle, Chicago, founder of the association, was named executive director of blindness prevention activities. Mrs. Gradle is a former executive director of the Illinois Society for the Prevention of Blindness. The congress was attended by 1,200 delegates from 22 nations; its next meeting will be in Santiago, Chile, in Jan., 1956.

Southeastern Allergy Association.—This association will hold its annual meeting March 21-22 at the Bon Air Hotel in Augusta, Ga., under the presidency of Dr. Lester C. Todd. The program includes two symposiums, one on the allergic personality with Dr. Hal M. Davison, Atlanta, Ga., as moderator. Participants will be Drs. Lamar B. Peacock, Atlanta, William A. Thornhill Jr., Charleston, W. Va., and J. Asa Shield, Richmond, Va. The endocrine system will be discussed March 22 by Dr. James C. Overall, Nashville, Tenn., from the pediatric standpoint, and by Dr. Oscar Swineford, Charlottesville, Va., from the adult standpoint. The banquet will be held March 21 at 7:30 p. m.

Gibbs Memorial Prize.—The New York Academy of Medicine has a sum of \$2,000 available in 1952 under the Edward N. Gibbs Memorial Prize for original research in diseases of the kidney. This is a grant-in-aid and is not for work already done. Candidates must be physicians who have been graduated at least three years and are residents of the United States. They shall submit evidence of research already performed and protocols of proposed research on the physiology of kidney function, etiology, pathology, or new methods of treatment of diseases of the kidney. Applications with the required evidence should be mailed prior to April 15 to Dr. Robert F. Loeb, Chairman, The Gibbs Prize Committee, Presbyterian Hospital, 622 West 168 St., New York 32.

Openings for Study of Radiologic Pathology.—The Registry of Radiologic Pathology, sponsored by the American College of Radiology, the American Roentgen Ray Society, and the Radiological Society of North America at the Armed Forces Institute of Pathology, Washington, D. C., offers an appointment for study and correlation of the voluminous roentgenologic and pathological material at the institute under the supervision of skilled pathologists. Appointments begin on October 1, January 1, April 1, and July 1, alt for a period of six months each, and carry a stipend of \$250 per month. Applicants must have completed a minimum of two years of training in an approved residency in radiology, preferable with six months of pathology. Preference will be given to applicants who have completed an approved residency in radiology or are eligible for the Board of Radiology examination. For information apply to Dr. Aubrey O. Hampton, Secretary, Inter-Society Committee for the Registry of Radiological Pathology, Garfield Memorial Hospital, 10th and Florida Ave., N. W., Washington, D. C.

William Stewart Halsted Centennial.—The centenary celebration of the birth of Dr. William Stewart Halsted was held Feb. 7 at Johns Hopkins Hospital, Baltimore, in conjunction with meetings of the Society of University Surgeons, the Society of Clinical Surgery, and the Halsted Club. Dr. Emile F. Holman, San Francisco, presided at the centenary program. Detlev W. Bronk, Ph.D., president of Johns Hopkins University, opened the meeting. Papers were presented by some of the former associates of Dr. Halsted: Drs. James Mitchell, Samuel J. Crowe, Bertram M. Bernheim, Arthur M. Shipley, and Edwards A. Park, all of Baltimore; Willis D. Gatch, Indianapolis, and Frederick L. Reichert, San Francisco. Others who presented papers were

Drs. Alan M. Chesney, Warfield M. Firor, William F. Rienhoff Jr., Richard H. Follis Jr., all of Baltimore; Emil Goetsch, Brooklyn; Samuel C. Harvey, New Haven, Conn.; B. Noland Carter, Cincinnati; David H. Patey, London, England, and Miss Margaret Boise. The Halsted centennial dinner was held at the Lord Baltimore Hotel. After-dinner speakers were Dr. René Leriche, Paris, and Dr. Allen O. Whipple, New York. Dr. Halsted was the first head of the department of surgery established in 1889 at Johns Hopkins Hospital.

American Academy of Forensic Sciences.—The fourth annual meeting of this organization will be held March 6-8 at the Biltmore Hotel, Atlanta, Ga., under the presidency of Dr. Samuel A. Levinson, Chicago. Papers will be read on forensic pathology, toxicology, and psychiatry, and on police science at general sessions and at special section meetings. Additional subjects to be presented at the general sessions include:

Problems of Administration in a State-Wide Medical Examiners System, Geoffrey T. Mann, Richmond.

A Two Year Analysis of Cases Investigated in a State-Wide Medical Examiners System, Harold L. Beddoe, Richmond.

The Computation of Age in Medico-Legal Practice in India, H. S. Mehta, Bombay, India.

Age of Skeletal Remains, William E. B. Hall, Chambersburg, Pa.

The Detection of Blood, William E. B. Hall, Chambersburg, Pa.

Pitfalls in the Examination of the Offender in the Report to the Court, Lowell S. Selling, Orlando, Fla.

Feticide, Infanticide, Concealment of Birth or Death, Louis J. Regan, Los Angeles.

Perversion of Science in Criminal and Civil Investigations, Mr. Fred E. Inbau, Chicago.

Fraternity Proceedings, A Changing Concept, Mr. Sidney B. Schatkin, New York.

Mathematics Applied to the Lie Detector Test Analysis, Mr. Paul L. Wilhelm, Michigan City, Ind.

The St. Louis Metropolitan Police Department's Study of Sex Molestation Patterns for 1950, Mr. Arthur C. Meyers Jr., St. Louis, Part One; Val B. Satterfield, St. Louis, Part Two.

At the banquet Friday at 7 p. m., Mr. Eugene Cook, state attorney general of Georgia, will speak on "Forgotten Laws." All interested are urged to attend the meeting. Prof. Ralph Turner, Michigan State College, East Lansing, is academy secretary.

93,000 Accidental Deaths.—The National Safety Council, Chicago, reports that 93,000 persons were killed in accidents during 1951, and 9,100,000 were injured at an economic loss of \$8 billion. The death toll was 4,000 greater than in 1950.

Motor vehicle accidents were the nation's leading accident killer, with home accidents second. The motor vehicle death toll was the highest in a decade. Only three years—1936, 1937, and 1941—exceeded 1951's total of 37,500 traffic deaths. The 1951 all-accident death rate was 60.6 per 100,000 population. This is the second lowest rate on record, bettered only by the record low rate of 58.8 in 1950, and it is 21% under the rate of 76.3 for 1941. One out of every 17 persons in the United States suffered a disabling injury in 1951. The estimated economic loss of \$8 billion from accidents in 1951 covers both fatal and nonfatal accidents and includes wage losses, medical expense, and overhead costs of insurance for all accidents, production delays, damage to equipment in occupational accidents, and property damage from traffic accidents and fires. Falls, always a heavy killer, brought death to 18,500 persons in 1951; deaths from burns numbered 7,000; drownings totaled 6,200, and deaths by firearms 2,400. Catastrophes in which the toll was at least five lives occurred more frequently in 1951 than in 1950. Up to the closing days of 1951 the number of deaths in such catastrophes totaled about 1,800, according to the Metropolitan Life Insurance Company, an increase of about 300 over 1950. Five catastrophes in 1951 caused 50 or more deaths each: The December coal mine explosion in Illinois, a suburban train wreck in New Jersey, a crash by a nonscheduled plane in New Jersey, and two crashes by scheduled air transports, one in Colorado and the other in California. Six other catastrophes caused from 25 to 49 deaths.

In addition to the fatalities, 1951 traffic accidents caused about 1,300,000 nonfatal injuries, and property loss estimated at \$1.4 billion. Of the 45 states reporting complete motor vehicle deaths for the year, only 10 had decreases from 1950 while 34 had increases. Rhode Island led the 10 states showing reductions with a decrease of 19%. Among cities with more than 200,000 population, Akron, Ohio, had the largest reduction in fatalities, 48% below 1950. Jacksonville, Fla., was next with a 39% drop,

and Memphis followed with a 38% decrease. Forty-nine cities of 10,000 population or more completed the year without a traffic death. Ann Arbor, Mich., with a population of 48,300 was the largest city to achieve this record. Eau Claire, Wis., was second and Watertown, N. Y., was third.

The home accident death total in 1951 was about 27,000. Disabling injuries from home accidents numbered 4,000,000, and wage loss, medical expense, and the overhead costs of insurance totaled about \$600 million.

Deaths from occupational accidents totaled 16,000, about 3% more than in 1950. Disabling injuries from work accidents numbered about 2,000,000. Economic loss from occupational accidents totaled about \$2.6 billion. Coal mine deaths totaled 790 in 1951, 23% more than the 1950 figure. Railroad employee fatalities were 249 in the first eight months, an increase of 19%; and injuries for eight months were up 16% to a total of 15,407. Deaths to workers from all accident causes totaled 50,000; of these 16,000 occurred on the job and 34,000 off the job. This is a 5% increase from 1950. Injuries were about 4,600,000, representing a total time loss of 340,000,000 man-days.

Nine accidents occurred in domestic passenger-carrying operations of scheduled air transports. The passenger death rate per 100,000,000 passenger-miles in 1951, based on preliminary information, was 1.3, compared with 1.1 in 1950.

FOREIGN

Meeting of German Roentgen Society.—The congress of this society will meet April 28-30 at Wiesbaden under the chairmanship of Dr. Gerhard Hammer, Städt. Krankenanstalten, Strahleninstitut, Nürnberg, Flurstrasse 17. Subjects to be discussed will be the roentgenographic diagnosis of bone changes in diseases of the blood, radioactive isotopes in diagnosis, radiation therapy of diseases of the hemopoietic system, and radiobiologic investigations on radiation protection.

CORRECTION

Current Trends in Immunization.—In the article by Dr. Aims C. McGuinness in THE JOURNAL, Jan. 26, 1952, page 264, in the third line of the paragraph on scarlet fever, the words "negative Dick tests" should read "positive Dick tests."

MEETINGS

AMERICAN ACADEMY OF ALLERGY, Hotel Sherman, Chicago, Feb. 18-20.

Dr. Ben Z. Rappaport, 208 East Wisconsin Ave., Milwaukee 2, Secretary.

AMERICAN ACADEMY OF FORENSIC SCIENCES, Biltmore Hotel, Atlanta, Ga.,

March 6-8. Prof. Ralph F. Turner, Michigan State College Dept. of

Police Administration, East Lansing, Mich., Secretary.

AMERICAN ACADEMY OF GENERAL PRACTICE, Atlantic City, N. J., March

24-27. Mr. Mac F. Cahal, 406 West 34th St., Kansas City 2, Mo., Execu-

tive Secretary.

AMERICAN ASSOCIATION OF ANATOMISTS, Providence, R. I., March 19-21.

Dr. Normand L. Hoerr, 2109 Adelbert Road, Cleveland 6, Secretary.

AMERICAN ASSOCIATION OF PATHOLOGISTS AND BACTERIOLOGISTS, New York,

April 10-12. Dr. Alan R. Moritz, 2085 Adelbert Road, Cleveland 6,

Secretary.

AMERICAN ASSOCIATION OF RAILWAY SURGEONS, Drake Hotel, Chicago,

April 1-3. Dr. Chester C. Guy, 5800 Stony Island Ave., Chicago 37,

Secretary.

AMERICAN COLLEGE OF ALLERGISTS, William Penn Hotel, Pittsburgh, April

7-9. Dr. Fred W. Wittich, 423 LaSalle Medical Bldg., Minneapolis 2,

Secretary.

AMERICAN COLLEGE OF SURGEONS, SECTIONAL MEETINGS:

Quebec, Can., Chateau Frontenac, Feb. 18-19. Dr. Paul A. Poliquin,

71 St. Ann St., Quebec, Can., Chairman.

Minneapolis, Radisson Hotel, March 24-26. Dr. Harvey Nelson, 78 South

9th St., Minneapolis 2, Chairman.

Tucson, Ariz., Pioneer Hotel, April 7-9. Dr. Meade Clyne, 110 South

Scott St., Tucson, Chairman.

Vancouver, B. C., Vancouver Hotel, March 31-April 4. Dr. J. Russell

Neilson, 925 West Georgia St., Vancouver, B. C., Chairman.

AMERICAN CONGRESS ON OBSTETRICS AND GYNECOLOGY, Netherlands-Plaza

Hotel, Cincinnati, March 31-April 4. Dr. Luella E. Nadelhoffer, 116

South Michigan Ave., Chicago 3, Secretary.

AMERICAN PSYCHOSOMATIC SOCIETY, Chicago, March 29-30. Dr. Frederick

C. Redlich, 551 Madison Avenue, New York 22, Secretary.

CENTRAL SURGICAL ASSOCIATION, Toronto, Can., March 6-8. Dr. James T.

Priestley, 102 Second Avenue S.W., Rochester, Minn., Secretary.

CHICAGO MEDICAL SOCIETY ANNUAL CLINICAL CONFERENCE, Palmer House,

Chicago, March 4-7. Dr. Walter C. Bornemeier, 86 East Randolph St.,

Chicago 1, Secretary.

MICHIGAN CLINICAL INSTITUTE, Book-Cadillac Hotel, Detroit, March 12-14. Dr. H. G. Cummings, 606 Townsend St., Lansing 15, Chairman.

MISSOURI STATE MEDICAL ASSOCIATION, Hotel Jefferson, St. Louis, March 30-April 2. Dr. H. E. Petersen, 634 North Grand Blvd., St. Louis 3, Secretary.

NATIONAL CONFERENCE ON RURAL HEALTH, Shirley-Savoy Hotel, Denver, Feb. 28-Mar. 1. Dr. F. S. Crockett, 535 North Dearborn St., Chicago 10, Chairman.

NEW ORLEANS GRADUATE MEDICAL ASSEMBLY, Municipal Auditorium, New Orleans, March 10-13. Dr. Woodward D. Beacham, 1430 Tulane Ave., Room 105, New Orleans 12, Secretary.

NORTH PACIFIC SOCIETY OF INTERNAL MEDICINE, Portland, Ore., March 22. Dr. R. L. King, 1115 Terry Ave., Seattle 1, Secretary.

PACIFIC COAST SURGICAL ASSOCIATION, Del Monte, Calif., Feb. 26-29. Dr. Carleton Mathewson Jr., Stanford University Hospital, San Francisco, Secretary.

PIEDMONT PROCTOLOGIC SOCIETY, Charlotte, N. C., March 29-30. Dr. B. Richard Jackson, 224 Hillsboro St., Raleigh, N. C., Secretary.

POST GRADUATE INSTITUTE OF THE PHILADELPHIA COUNTY MEDICAL SOCIETY, Bellevue-Stratford Hotel, Philadelphia, April 1-4. Dr. Thomas M. Durant, 301 South 21st St., Philadelphia 3, Director.

SOUTHEASTERN ALLERGY ASSOCIATION, Bon Air Hotel, Augusta, Ga., March 21-22. Dr. Katharine B. MacInnis, 1515 Bull St., Columbia 49, S. C., Secretary.

SOUTHEASTERN SECTION, AMERICAN UROLOGICAL ASSOCIATION, Boca Raton, Fla., April 2-5. Dr. Russell B. Carson, Sweet Bldg., Fort Lauderdale, Fla., Secretary.

SOUTHEASTERN SURGICAL CONGRESS, Atlanta, Ga., March 10-13. Dr. Benjamin J. Beasley, 701 Hurt Bldg., Atlanta 3, Ga., Secretary.

SOUTHWEST ALLERGY FORUM, Hotel Baker, Dallas, Texas, March 2-4. Dr. James Holman, Medical Arts Bldg., Dallas, Secretary.

TENNESSEE STATE MEDICAL ASSOCIATION, Andrew Johnson Hotel, Knoxville, April 7-9. Mr. V. O. Foster, 504 Doctors Bldg., Nashville 3, Executive Secretary.

TRI-STATES MEDICAL ASSOCIATION OF THE CAROLINAS AND VIRGINIA, Patrick Henry Hotel, Roanoke, Va., Feb. 18-19. Dr. James N. Northington, 306 North Tryon St., Charlotte 2, N. C., Secretary.

UNITED STATES-MEXICO BORDER PUBLIC HEALTH ASSOCIATION, Monterrey, Nuevo Leon, Mexico, March 17-19. Dr. J. C. Ellington, 314 U. S. Court House, El Paso, Texas, Secretary.

WESTERN SOCIETY OF ELECTRO-ENCEPHALOGRAPHY, Del Monte Lodge, Pebble Beach, Calif., March 2-3. Dr. Nicholas A. Bercel, 450 North Bedford Drive, Beverly Hills, Calif., Secretary.

INTERNATIONAL

AUSTRALASIAN MEDICAL CONGRESS, Melbourne Victoria, Australia, Aug. 22-30. Dr. C. H. Dickson, Medical Society Hall, 426 Albert St., East Melbourne, Victoria, Australia, Hon. General Secretary.

COMMONWEALTH AND EMPIRE HEALTH AND TUBERCULOSIS CONFERENCE, Central Hall, London, England, July 8-13. Dr. J. H. Harley Williams, Tavistock House North, Tavistock Sq., London, W.C.1, England, Secretary General.

CONGRESS OF THE INTERNATIONAL DIABETES FEDERATION, Leyden, Netherlands, July 7-12. Dr. F. Gerritzen, 33, Prinsegracht, The Hague, Netherlands, Secretary.

EUROPEAN CONGRESS OF CARDIOLOGY, University of London, Bloomsbury, W.C.1, England, Sept. 10-12. Dr. K. Shirley Smith, 35 Wimpole St., London, W.1, England, Secretary.

EUROPEAN SOCIETY OF CARDIOVASCULAR SURGERY, Strasbourg, France, Oct. 3-4. Sir James Learmonth, Department of Surgery, University New Buildings, Edinburgh 8, Scotland.

INTERAMERICAN CARDIOLOGICAL CONGRESS, Buenos Aires, Argentina, Aug. 31-Sept. 7. Dr. Blas Moia, Larrea 1132, Buenos Aires, Argentina, Secretary-General.

INTER-AMERICAN CONGRESS OF PUBLIC HEALTH, Havana, Cuba, Sept. 27-Oct. 1. Pan-American Sanitary Bureau, 2001 Connecticut Ave., Washington, D. C.

INTER-AMERICAN CONGRESS OF RADIOLOGY, Mexico City, Mexico, Nov. 2-6. Dr. Guido Torres Martinez, Marsella No. 11, Mexico, D.F., Secretary-General.

INTERNATIONAL COLLEGE OF SURGEONS, Madrid, Spain, May 20-24. Dr. Max Thorek, 850 West Irving Park Road, Chicago, Ill., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF COMPARATIVE PATHOLOGY, Madrid, Spain, May 4-11. Prof. Carda-Aparici, Calle Fernando VI.8, Madrid, Spain, Secretary.

INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY, London, England, July 21-26. Dr. Gordon B. Mitchell-Heggs, 5, Lisle St., London, W.C.2, England, General Secretary.

INTERNATIONAL CONGRESS ON DIABETES, Leyden, The Netherlands, July 7-12. Dr. F. Gerritzen, 33, Prinsegracht, The Hague, Netherlands.

INTERNATIONAL CONGRESS OF HAEMATOLOGY, Mar del Plata, Argentina, Sept. 21-26. Dr. Carlos Reussi, Anchorena 1710, Buenos Aires, Argentina, Secretary.

INTERNATIONAL CONGRESS OF HEALTH TECHNICIANS, Palais de la Mutualité, Paris, France, June 9-14. Secretariat General, 6 Square Desaix, Paris XV^e, France.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Friends House, London, N.W.1, Eng. Sept. 15-18. Sir Harold Boldero, 12 Pall Mall East, London, S.W.1, England, Secretary.

INTERNATIONAL CONGRESS OF LEGAL AND SOCIAL MEDICINE, Berne, Switzerland, April 15-18. Prof. J. Detling, 20, Buhlstrasse, Berne, Switzerland.

INTERNATIONAL CONGRESS ON NEUROPATHOLOGY, Rome, Italy, Sept. 8-13. Dr. Armando Ferraro, 722 W. 168th St., New York, N. Y., U. S. A., Secretary General.

INTERNATIONAL CONGRESS OF OTO-NEURO-OPHTHALMOLOGY, Lisbon, Portugal, April 22-26. Prof. Diogo Furtado, Servico de Neurologia, Hospital dos Capuchos, Lisbon, Portugal, General Secretary.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE, London, England, July 14-19. Dr. A. C. Boyle, 45, Lincoln's Inn Fields, London, W.C.2, England, Hon. Secretary.

INTERNATIONAL CONGRESS FOR THERMALISM AND CLIMATOTHALASSOTHERAPY, Nice-Cannes, France, April 3-8.

INTERNATIONAL SOCIETY OF GEOGRAPHIC PATHOLOGY, Liège, Belgium, July 15-18. Dr. Fred C. Roulet, Habelstr. 24, Basel, Switzerland, Secretary General.

INTERNATIONAL UNION AGAINST TUBERCULOSIS, Rio de Janeiro, Brazil, Aug. 24-27. Prof. Etienne Bernard, 66 Blvd. St. Michel, Paris 6^e, France, Secretary-General.

LATIN AMERICAN CONGRESS OF PHYSICAL MEDICINE, Panama City, R. P., Feb. 24-29. Dr. Cassius Lopez de Victoria, 176 East 71st St., New York, N. Y., U. S. A., Executive Director.

NEURORADIOLOGIC SYMPOSIUM, Stockholm, Sweden, Sept. 17-20. Docent Ake Lindbom, Symposium Neuroradiologicum, Serafimerlasarettet, Stockholm K., Sweden, Secretary.

PAN-AMERICAN CONGRESS OF GASTROENTEROLOGY, Mexico City, D.F., May 11-17. Dr. R. Flores-Lopez, Calle Dr. Balmis, No. 148, Mexico City, D.F., Secretary.

PAN-EUROPEAN CONGRESS OF GASTROENTEROLOGY, Bologna, Florence and Rome, Italy, April 20-26. Prof. Guido Bassi, Policlinic of St. Orsola, Bologna, Italy, Secretary.

WORLD MEDICAL ASSOCIATION, Athens, Greece, Oct. 12-16. Dr. Louis H. Bauer, 2 East 103d St., New York 29, N. Y., Secretary General.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Part II*, April 21-22; *Parts I and II*, June 16-18 or June 23-25; *Part I*, September. All centers where there are five or more candidates. Exec. Sec., Dr. John P. Hubbard, 225 S. 15th St., Philadelphia 2.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: Various Locations, July 18. Final date for filing application was Jan. 18. Sec., Dr. C. B. Hickcox, 80 Seymour St., Hartford 15.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written*. Various centers. March 1952. *Oral*. Chicago, May 1952. Final date for filing application was Feb. 1, 1952. Candidates for these tests must have completed three years of approved training prior to July 1, 1952. Sec., Dr. George M. Lewis, 66 E. 66th St., New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written*. Various centers and overseas, Oct. 20. Closing date for the acceptance of applications for the written examination will be May 1. *Oral*. Cleveland, April 17-19; Chicago, June 5-7, San Francisco, September or October; New York City, November or December. Exec. Sec.-Treas., Dr. William A. Werrell, 1 West Main Street, Madison 3.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral*. Chicago, May 1952. Final date for filing applications for the May 1952 examination was Jan. 1. Sec., Dr. W. J. German, 789 Howard Ave., New Haven 4, Conn.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Oral*. Chicago, June 9-13, 1952. Final date for filing application was Feb. 1, 1952. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Practical*. Philadelphia, May 29-June 3; Chicago, Oct. 6-10 and New York City, June 6-10, 1953. Sec., Dr. Edwin B. Dunphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF OTOLARYNGOLOGY. Toronto, May 13-17; Chicago, Oct. 6-10. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PEDIATRICS: *Oral*. St. Louis, Mo., Mar. 21-23; Washington, D. C., May 3-5; San Francisco, late June; Chicago, October and Boston, late November. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION: *Parts I and II*. Chicago, June 8 and 9. Sec., Dr. Robert L. Bennett, Georgia Warm Springs Foundation, Warm Springs, Ga.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral and Written*. St. Louis, May 17-19. Sec., Dr. Bradford Cannon, 4647 Pershing Ave., St. Louis 8.

AMERICAN BOARD OF PREVENTIVE MEDICINE AND PUBLIC HEALTH. *Written*. Berkeley, Calif., Minneapolis, New Orleans and Baltimore. April 18. Sec., Dr. Ernest L. Stebbins, 615 N. Wolfe St., Baltimore.

AMERICAN BOARD OF PROCTOLOGY. *Part I*. Kansas City, Minneapolis, Philadelphia and San Francisco. May 3. Examination includes both oral and written examinations in the basic sciences. *Dates and places tentative*. Sec., Dr. Louis A. Buie, 102-110 2d Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: Chicago, June 13-14. Final date for filing applications is March 15. New York City, Dec. 15-16. Final date for filing applications is Sept. 15. Sec.-Treas., Dr. David A. Boyd, Jr., 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Oral*. Spring 1952. Final date for filing application was Dec. 31. Sec., Dr. B. R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written*. Various Centers. March 1952. Final date for filing application was Dec. 1, 1951. The following written examination will be given in October 1952. Sec., Dr. J. Stewart Rodman, 225 S. 15th St., Philadelphia.

BOARD OF THORACIC SURGERY: Various parts of the country. *Written*. Feb. 29, 1952. Final date for filing application is Jan. 15. Sec., Dr. William M. T. for Ave., Del. 2.

DEATHS

Fitzpatrick, Charles Patrick, Lynwood, Calif.; born in Napanee, Ontario, Canada, in 1895; University of Toronto Faculty of Medicine, Toronto, Canada, 1920; member of the American Medical Association and the American Psychiatric Association; specialist certified by the American Board of Psychiatry and Neurology; at one time clinical director of Butler Hospital in Providence, R. I., and superintendent of State Hospital for Mental Diseases at Howard, R. I.; medical superintendent of Provincial Mental Institute in Edmonton, Alberta, Canada, from 1929 to 1931; resident physician at the Compton Sanitarium from 1944 to 1947; lecturer in abnormal psychiatry at Brown University in Providence, R. I. from 1935 to 1943, and special lecturer of social psychiatry at Simmons College, Boston, 1938-1939; died recently, aged 56, of hypertensive arteriosclerotic heart disease.

Croson, Franklin Roy ☉ Clay Center, Kan.; born in Aledo, Ill., Sept. 5, 1892; Northwestern University Medical School, Chicago, 1918; for many years a member of the council, immediate past president and formerly secretary of the Kansas Medical Society; the Student Loan Fund for the University of Kansas School of Medicine was established by the state society during his presidency and the fund will permanently be known as the Dr. Croson Memorial Student Loan Fund; past president and secretary of the Clay County Medical Society; on the staff of the Clay Center Municipal Hospital; active in civic affairs and especially interested in the Rotary Club, having attended a number of meetings of Rotary International; honorary member of the Clay Center Club, of which he had been president in 1931-1932; died in St. Joseph's Hospital, Concordia, Nov. 7, aged 59, of aortic aneurysm.

Ordway, Mabel Dyer ☉ Boston; born in Boston July 29, 1874; Tufts College Medical School, Boston, 1905; specialist certified by the American Board of Psychiatry and Neurology; member of the New England Women's Medical Society, Association for Research in Nervous and Mental Diseases, American Psychiatric Association, of which she had been secretary, and New England Society of Psychiatry; became a member of the staff of the Channing Sanitarium, Brookline in 1908; later a staff member at Massachusetts General Hospital, Boston City Hospital, and New England Hospital; superintendent of Glenside Hospital, which she founded in 1909; died Nov. 26, aged 77, of arteriosclerotic heart disease.

Gelston, Clain Fanning ☉ San Francisco; born in Bay City, Mich., Dec. 7, 1890; University of California Medical School, San Francisco, 1915; assistant clinical professor of pediatrics at his alma mater; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; served in France during World War I; decorated by the French government with the Medaille des Epidemies; in 1942 honorably discharged as a major in the medical reserve corps of the U. S. Army; chief of the department of pediatrics at the Children's Hospital, where he was at one time medical director; consulting pediatrician, Mount Zion Hospital and Shriners' Hospital for Crippled Children; visiting pediatrician, University of California and Stanford University hospitals; died Nov. 28, aged 60.

Schenk, Erwin ☉ Des Moines; born in Waterloo, Iowa, Jan. 3, 1871; New York Homeopathic Medical College and Hospital, New York, 1900; an Associate Fellow of the American Medical Association; served as a member and secretary of the Iowa State Board of Medical Examiners; at one time professor of theory and practice of medicine at the State University of Iowa College of Homeopathic Medicine in Iowa City; affiliated with Iowa Lutheran Hospital, Broadlawns Polk County Hospital, and the Iowa Methodist Hospital, where he died Nov. 14, aged 80, of bronchopneumonia, prostatic hypertrophy, and cerebral arteriosclerosis.

Arthur, William Richard, Hampton, Iowa; State University of Iowa College of Medicine, Iowa City, 1907; died in the Lutheran Hospital Nov. 27, aged 73, of cerebrovascular accident, arterial hypertension, and nephrosclerosis.

Brumwell, Dorus, King City, Calif.; Kentucky School of Medicine, Louisville, 1889; died Nov. 19, aged 92, of arteriosclerosis and epithelioma.

Calhoun, Grant ☉ Seattle; Cooper Medical College, San Francisco, 1898; an Associate Fellow of the American Medical Association; in 1909 president of the King County Medical Society; formerly superintendent of Morningside Hospital; died in Seattle General Hospital Oct. 9, aged 78, of carcinoma of the prostate.

Camoegas, Joao Jose da Conceicao ☉ Taunton, Mass.; Universidade de Lisboa Faculdade de Medicina, Portugal, 1925; at one time minister of education in Portugal and a member of the Portuguese Legislative Assembly; on the staff of Morton Hospital; died Nov. 11, aged 64, of coronary thrombosis.

Connor, Robert W. ☉ Owensboro, Ky.; University of Louisville School of Medicine, 1915; affiliated with Owensboro-Daviess County Hospital; died Oct. 1, aged 65, of malignant hypertension.

Conrad, Overton Llewellyn, Breeding, Ky.; Hospital College of Medicine, Louisville, Ky., 1899; veteran of the Spanish-American War; died Nov. 4, aged 78, of myocardial infarction.

Crawford, Jennings ☉ Cedar Rapids, Iowa; Johns Hopkins University School of Medicine, Baltimore, 1909; member of the American Urological Association; died Nov. 29, aged 68, of acute myocardial infarction and coronary arteriosclerosis.

Deig, Albert A., Louisville, Ky.; Louisville Medical College, 1894; died Oct. 7, aged 90.

Dresel, Kurt Max, New York; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1917; member of the American Medical Association; died Oct. 30, aged 59, of coronary infarction.

Edmunds, George Joseph, Pittsburgh; Medico-Chirurgical College of Philadelphia, 1910; served as chief medical examiner for the Baltimore and Ohio Railroad; died in Mercy Hospital Nov. 17, aged 66, of pneumonia.

Evans, Kline Wilborn, Columbia, Tenn.; St. Louis University School of Medicine, 1944; member of the American Medical Association; served during World War II; on the staff of the Kings Daughters Hospital; died recently, aged 32, of poliomyelitis.

Fellers, Andrew Burns, Palisade, Neb.; Denver and Gross College of Medicine, 1905; member of the American Medical Association; died Nov. 22, aged 72.

Fleming, Carl Marshall ☉ Rushville, Ill.; St. Louis College of Physicians and Surgeons, 1906; past president of the Schuyler County Medical Society; died in Mercy Hospital, Des Moines, Iowa, Nov. 25, aged 74, of cerebral hemorrhage.

Fuller, Nathaniel Hall, Cuba, N. Y.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1901; member of the American Medical Association; past president of the Allegany County Medical Society; formerly county coroner; died Nov. 3, aged 76.

Gamble, Robert Anderson ☉ Madrid, Iowa; St. Louis College of Physicians and Surgeons, 1907; died in Iowa Lutheran Hospital, Des Moines, Nov. 22, aged 72, of coronary thrombosis.

Girdner, William Haywood, Abernathy, Texas; Chattanooga (Tenn.) Medical College, 1905; member of the American Medical Association; died recently, aged 79, of cerebral hemorrhage.

Gore, Randolph Cook, Loneoak, Ky.; Barnes Medical College, St. Louis, 1898; member of the American Medical Association; died Nov. 4, aged 76, of cerebral hemorrhage and arteriosclerosis.

Gullinger, Lowry M., Andover, Ohio; Chicago Homeopathic Medical College, 1898; died Nov. 14, aged 83.

Head, Luther Jerrell, Penola, Va.; University College of Medicine, Richmond, 1903; for many years member of the county board of health and county school board; died in Johnston-Willis Hospital, Richmond, Nov. 8, aged 85.

Johnston, William Harrison, Des Moines, Iowa; University of Illinois College of Medicine, Chicago, 1947; member of the American Medical Association; served during World War II; resident at the Veterans Administration Center, where he died Nov. 20, aged 29, of coronary occlusion.

Junger, Emil Charles, Soldier, Iowa; Sioux City College of Medicine, 1902; died in Lutheran Hospital, Sioux City, Nov. 23, aged 77, of cerebral thrombosis and hypertension.

Justice, Gaston B., Marion, N. C.; Atlanta College of Physicians and Surgeons, 1907; veteran of the Spanish-American War; died Nov. 4, aged 71, of coronary occlusion.

Kibler, John Charles & **Corry, Pa.**; Baltimore University School of Medicine, 1905; served during World War I; examining physician for the local school district for many years; on the staff of Corry Memorial Hospital; local physician for the Erie Railroad; died Nov. 25, aged 72, of arteriosclerotic heart disease.

Klein, Isaac, Boston; Tufts College Medical School, Boston, 1906; for many years physician for the Massachusetts State Boxing Commission; died Nov. 11, aged 67, of carcinoma of the liver.

Luehrmann Bernard H. & **Dyersville, Iowa**; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1900; affiliated with St. Joseph Mercy and Xavier hospitals in Dubuque; died Nov. 28, aged 76, of carcinoma of the larynx.

McKibben, James Thompson, Cincinnati; Medical College of Ohio, Cincinnati, 1891; died in Bethesda Hospital Nov. 11, aged 84, of diabetes mellitus and pyelonephritis.

Markey, James Bernie, Hopkinsville, Ky.; University of Louisville Medical Department, 1909; superintendent of the Western State Hospital; member of the American Psychiatric Association; died Nov. 2, aged 73.

Mayers, Howard Doane, Fall River Mills, Calif.; Northwestern University Medical School, Chicago, 1934; member of the American Medical Association; certified by the National Board of Medical Examiners; died near San Jose, Nov. 2, aged 50, in an automobile accident.

Mulloy, Joseph Jerry, Stephenville, Texas; Memphis (Tenn.) Hospital Medical College, 1893; Marion-Sims College of Medicine, St. Louis, 1899; member of the American Medical Association; died recently, aged 78, of heart disease.

Murphy, Frank Graham, Mason City, Iowa; Howard University College of Medicine, Washington, D. C., 1893; died Nov. 17, aged 84, of chronic myocarditis and arteriosclerotic heart disease.

Nevill, Paul Lee, Saluda, S. C.; Southern College of Medicine and Surgery, Atlanta, 1914; died Nov. 9, aged 63, of coronary thrombosis.

Padget, Paul & **Fort Howard, Md.**; Johns Hopkins University School of Medicine, Baltimore, 1927; assistant professor of medicine at his alma mater; formerly instructor in medicine at the University of Maryland School of Medicine; specialist certified by the American Board of Internal Medicine; served during World War II; chief of the medical service at the Veterans Administration Hospital; died suddenly Oct. 31, aged 46.

Peck, John Dickinson, Summersville, W. Va.; Duke University School of Medicine, Durham, N. C., 1942; member of the American Medical Association; certified by the National Board of Medical Examiners; served in the medical reserve corps of the U. S. Army in England and Italy during World War II; killed in an automobile accident, Dec. 23, aged 34.

Pelle, Frank A., Wilmington, Ohio; Medical College of Ohio, Cincinnati, 1897; died in McMillen Sanitarium, Columbus, November 2, aged 83, of cerebral hemorrhage and cerebral arteriosclerosis.

Pinkerton, Harry Blaine, Buffalo; Chicago Homeopathic Medical College, 1903; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1906; member of the American Medical Association; fellow of the American College of Surgeons; died November 29, aged 69, of a heart attack.

Reilly, Joseph A., Kansas City, Mo. (licensed in Missouri in 1898); died in Peralta Hospital, Oakland, November 10, aged 70, of cardiac failure following left pneumonectomy for pulmonary tuberculosis.

Richards, Dickinson Carlyle, Newark, N. J.; Creighton University School of Medicine, Omaha, 1921; died Nov. 30, aged 58.

Richardson, Robert W., Duncan, Okla. (licensed in Oklahoma in 1928); served as city health officer; died Nov. 1, aged 80, of a heart attack.

Ross, Allan, Los Angeles; Western University Faculty of Medicine, London, Ont., Canada, 1908; died November 11, aged 65, of coronary thrombosis.

Rowles, John Franklin & **Mahaffey, Pa.**; Medico-Chirurgical College of Philadelphia, 1904; died in Clearfield (Pa.) Hospital November 15, aged 82.

Runde, Frederick William & **St. Louis**; Marion-Sims College of Medicine, St. Louis, 1898; affiliated with Missouri Baptist Hospital; died Nov. 20, aged 77, of myocardial infarction.

Schneller, John Johnson, Catasauqua, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1938; member of the American Medical Association; member of the Civil Service Board; served during World War II; deputy coroner; on the staff of Sacred Heart Hospital in Allentown; director of the Lehigh National Bank; died in University of Pennsylvania Hospital, Philadelphia, Nov. 22, aged 37, of cerebral hemorrhage.

Smoot, Charles E., Richmond, Ky.; Chicago Homeopathic Medical College, 1899; died Oct. 23, aged 76, of coronary thrombosis.

Southall, Oliver Samuel, Millville, Pa.; Temple University School of Medicine, Philadelphia, 1929; member of the American Medical Association; on the staff of the Bloomsburg (Pa.) Hospital; served during World War I; died Nov. 23, aged 54.

Trainor, Morgan Xenophon Lewis & **Chicago**; Chicago Medical School, 1921; died in Illinois Central Hospital November 24, aged 66, of cerebral hemorrhage and hypertension.

Weber, James August, Olney, Ill.; St. Louis University School of Medicine, 1912; member of the American Medical Association; one of the founders and owners of Olney Sanitarium, where he died Nov. 13, aged 64, of complications following an operation for carcinoma of the lung.

Westervelt, William Alfred, Tempe, Ariz.; Medical College of Indiana, Indianapolis, 1894; veteran of the Spanish-American War; died Oct. 30, aged 81, of cerebral hemorrhage.

Wickham, Archibald B. & **Phoenix, Ariz.**; Detroit College of Medicine, 1904; member of the Michigan State Medical Society, American College of Chest Physicians, American Trudeau Society, and the Radiological Society of North America; formerly practiced in Detroit; served as medical director of the East Lawn Sanatorium in Northville, Mich.; died October 27, aged 75, of coronary occlusion and arteriosclerosis.

Zartman, Luke V. & **Columbus, Ohio**; Johns Hopkins University School of Medicine, Baltimore, 1910; clinical professor of surgery at the Ohio State University College of Medicine; on the staffs of Ohio State University Hospital and St. Francis Hospital, where he died Nov. 27, aged 67, of myocardial infarction.

Zivnuska, Jaros F. & **Milwaukee**; Milwaukee Medical College, 1905; past president of the Wisconsin Academy of Surgery; past president and, since Jan., 1951, honorary member of the staff of St. Luke's Hospital; member of the board of directors of Johnston Emergency Hospital; died Nov. 24, aged 71, of carcinoma.

GOVERNMENT SERVICES

DEPARTMENT OF DEFENSE

The Number of Physicians Commissioned.—The Armed Forces Medical Policy Council in the office of the Secretary of Defense has announced that as of Jan. 1, 1952, 5,478 physicians and 2,296 dentists who registered in priority 1 category under Public Law 779 have received commissions in the armed forces. Of this number, 4,476 physicians and 2,201 dentists have been ordered to active duty. The remaining 1,002 physicians and 95 dentists are, for the most part, persons under current consideration for call to active duty or those whose call has been temporarily delayed because of their essentiality.

Public Law 779, which was passed in September, 1950, and is sometimes called the "doctor draft," established four categories under which medical and dental specialists were required to register and also established the order of priority of these categories for induction purposes.

Physicians and dentists registered in priority 1 category are those who participated in an ASTP or V-12 program or were deferred from service during World War II to attend school at their own expense, and who have served less than 90 days in the armed forces, Coast Guard, or U. S. Public Health Service subsequent to the completion of their medical or dental education. To date, the armed forces have not had to go beyond the priority 1 category.

Personal.—Dr. Randolph T. Major, scientific director, Merck & Company, Rahway, N. J., has been named chairman of the Research and Development Board Committee on Chemical Warfare. Dr. Major has served the Research and Development Board in various capacities since 1948.

AVY

Rear Admiral Groesbeck Jr. Honored.—At a dinner, Jan. 29, at the Naval Medical Center, Bethesda, Md., Rear Adm. Bertram Groesbeck Jr., assistant chief of the Navy's Bureau of Medicine and Surgery for Aviation and Operational Medicine, was honored when the Theodore C. Lyster Award for 1951 of the Aero Medical Association was presented to him. The award is presented each year to the person who contributes most to the advancement in the field of aviation medicine. Selection of Admiral Groesbeck to receive the award was made at the annual meeting of the association held May 14-16, 1951, at Denver, Colo.

Long-Range Research Program.—A conference was held Feb. 6-7 at the Bureau of Medicine and Surgery, Washington, D. C., to formulate a long-range program of medical research in the Naval Medical Department; to collaborate the long-range plan with the Bio Sciences Division of the Office of Naval Research; and to review research projects that have been, or are being, carried out under the auspices of the Bureau of Medicine and Surgery.

Rear Adm. Bertram Groesbeck Jr., assistant chief of the Bureau for Research and Medical Specialties, was chairman of the conference. Rear Adm. H. W. Smith, MC, retired inactive, presented a paper on research progress in the Navy Medical Department, and Dr. Howard T. Karsner, research advisor to the Surgeon General, spoke on the relation of the Navy Medical Research Laboratories to the National Research Council, the Armed Forces Institute of Pathology, and the Armed Forces Medical Library. Representatives of the various Navy medical research laboratories gave résumés of work being carried on at their activities. The delegates met with the newly formed Committee on Naval Medical Research, Division of Medical Sciences, National Research Council, at which meeting, Dr. Detlev Bronk, president of the National Academy of Science, spoke on medical research in the Navy.

AIR FORCE

Aviation Medical Examiners.—Diplomas were given to 70 medical officers, including 7 foreign officers, January 19 at graduation exercises for the Aviation Medical Examiner Class at the Air Force School of Aviation Medicine, Randolph Field, Texas. The graduation address was delivered by Dr. Ernest L. Stebbins, dean, School of Hygiene and Public Health at Johns Hopkins University, Baltimore. The foreign officers in the class were from Greece, Italy, Thailand, and Denmark. This was the last aviation medical examiner class to graduate after but six weeks of formal training. The aviation medical examiner course reverts to its standard 11 weeks' duration. More than 100 medical officers reported to the school January 27 to attend the next class.

PUBLIC HEALTH SERVICE

New Manager of the Lexington, Ky. Hospital.—Dr. Kenneth W. Chapman has been appointed medical officer in charge of the U. S. Public Health Service Hospital, at Lexington, Ky., succeeding Dr. Victor H. Vogel, who is now assigned to the American Embassy in Paris, France, as medical officer in charge, U. S. Public Health Service, Foreign Quarantine activities. In his new position Dr. Chapman will be responsible for the management of a 1,400 bed hospital especially equipped to treat narcotic addicts as well as patients with neuropsychiatric disorders who are beneficiaries of the Public Health Service. This hospital trains psychiatrists and psychiatric nursing personnel and conducts research on narcotic drugs and addiction to them. Dr. Chapman is a psychiatrist certified by the American Board of Psychiatry.

Training in Treatment of Arthritis.—A program of clinical traineeships in the prevention, diagnosis, and treatment of arthritis and the metabolic diseases has been established at the National Institute of Arthritis and Metabolic Diseases. The purpose of the first group of awards is to improve the competency of physicians in the treatment and rehabilitation of arthritis patients. Applicants must not be over 40 years of age, must be American citizens, graduates of an approved medical school, and have completed a one-year internship in an approved hospital. The stipend for trainees without dependents is \$3,000 per year; with dependents, \$3,600. Trainees are placed in qualified institutions of their choice. For information write to Chief, Extramural Programs, National Institute of Arthritis and Metabolic Diseases, Bethesda 14, Md.

Aid in Epidemics.—The Public Health Service epidemiologists assisted state and local health departments in dealing with 88 epidemics and disease outbreaks and one disaster during 1951, the Public Health Service, has announced. Epidemiological and other emergency assistance was provided by the service in 16 outbreaks of poliomyelitis, 11 of infectious hepatitis, 6 of gastroenteritis, and 55 other epidemics or individual cases of about 25 other diseases. Assistance was also provided in connection with the Kansas City flood.

The Epidemic Intelligence Service has proven so successful the Surgeon General said, that the Communicable Disease Center now is recruiting an additional 20 to 25 young medical officers in order to double its forces in the field.

Doctor Geyer Awarded Medal.—Dr. Alfred Geyer, medical director of the U. S. Public Health Service Division in Seattle, was awarded the Third Antarctic Service Expedition Medal Dec. 12 in a ceremony at which the medal was presented by Captain R. E. Fielding, MC, USN, medical director for the Military Sea Transportation Service. Doctor Geyer received the medal for his service as medical officer on the icebreaker North Star during Rear Adm. Robert E. Byrd's expedition to the Antarctic region in 1939-1941.

FOREIGN LETTERS

DENMARK

Reform of Medical Curriculum.—The plans for the reform of the medical curriculum by the university faculties in Denmark have not been officially announced, but Prof. Erik Warburg, who participated in the planning, gave an account of its main features at a meeting held on Aug. 26 under the auspices of the Danish Medical Association. Broadly speaking, the time spent on the preliminary studies of physics, chemistry, anatomy, physiology, and biochemistry is to be shortened, and the time spent on the advanced subjects is to be lengthened, with better facilities for teaching to be made available. An anomalous state of affairs and an unsatisfactory influence on the medical profession may be produced by the diversity between the limits put on the entrance of students to the technical high school, the school of dentistry, the school of pharmacy, and the veterinary and agricultural high school and the comparatively fewer limits on the would-be entrants to the medical profession. Certain students rejected by the aforementioned schools turn to the medical profession as a last resort, with the result that it may admit a number of undesirable persons. In order to weed out these persons, high teaching and examination standards have been set for such preliminary subjects as physics and chemistry. It is proposed that the number of classes of inorganic chemistry shall be reduced by 33⅓% and those of organic chemistry by 10 to 20%, while students with a high mathematical rating will not have to pass examinations in physics.

At the other end of the medical curriculum, provision will be made for more teachers and more effective teaching, with special classes for teams of only 10 at a time in such subjects as physical examination and nursing. More teaching is to be provided in pediatrics, dermatology, psychiatry, medical psychology, mental hygiene, and epidemiology.

Why Do Doctors Become General Practitioners?—At the meeting held by the Danish Medical Association on Aug. 26, Dr. K. H. Backer gave an account of enquiries he has conducted among physicians, who were questioned as to their choice of general practice or specialization. Among 86 recently qualified physicians, there were 39.6% who planned to enter general practice, 5.8% who planned to do the same or to specialize, 32.6% who intended to specialize, 11.6% who aimed at research, and 10.4% who were undecided. Another group of 148 physicians, already established in general practice, were asked when they had determined to enter general practice. While 102 of them had made up their minds about this subject before their final examinations or soon afterward, there were as many as 46 who did not make this decision until more than three years after qualifying as physicians. In yet another group of 133 general practitioners, Dr. Backer discovered 71 who had tried to become specialists by means of hospital appointments. This observation has tempted him to cast a critical glance at the conditions under which junior hospital appointments are made. There seems to be a tendency in certain quarters to reserve hospital appointments for candidates likely to remain specialists, at the expense of others who are likely to enter or return to general practice. Dr. Backer suggests that in some cases the time spent between qualifying as a physician and going into general practice is poorly planned and excessively long. Here there is surely an opening for reform by the systematic anticipation of the needs of the prospective general practitioner.

The Danish National Association Against Tuberculosis.—Early in 1951 the Danish National Association Against Tuberculosis celebrated its 50 year jubilee, and in this connection it issued a *festskrift*, in which its many activities were reviewed. More recently it has issued an annual report covering the period April 1, 1950, to March 31, 1951. One of the most important activities of the association has been the voluntary examination of the public, and at the end of the year under review, nearly half a

million (444,488) persons had been examined; of these, 205,093 had been vaccinated with BCG vaccine. Nearly all who were found to be tuberculin negative consented to this measure voluntarily. The rapidly falling tuberculosis mortality, the lowest in Europe and perhaps in the world, is reflected in the dwindling number of new cases found in the course of mass examination. There was only one new case for every 2,131 persons examined in the age groups 1 to 6 and 15 to 34 years. This ratio was 1 to 1,509 for persons over the age of 35. These mass examinations were to have been completed in the course of the spring of 1952, but the public's appreciation of them has been such that they are not likely to be completed before December, 1952.

Diphtheria Vaccination in Copenhagen.—Ramon's method of vaccinating against diphtheria was started in September, 1941, in Copenhagen, where the disease was endemic at the time. Two years later, 100,000 children between the ages of 1 and 15 years, or about 80% of the children of this age, had been vaccinated. As pointed out by Dr. Knud Bojlén of the State Serum Institute in Copenhagen, vaccination against diphtheria has been continued in the city's national schools, and, by the end of the school year, 1947-1948, about 99% of the school children had been vaccinated. Since then there has been a slight decrease in this percentage, which was about 97 in the school year 1950-1951. During the last six years there has been a slow but steady rise in the number of children of the school-entry age who have not been vaccinated against diphtheria—an indication that perhaps both physicians and parents have become slack in this respect. But Dr. Bojlén regards the situation at the present time as satisfactory, and he notes that the percentage of diphtheria carriers in Copenhagen continues to fall. In 1944 it was as high as 5.8%, whereas in 1950 it was down to 0.6%, and it is probably still falling. But of course this does not imply that Copenhagen is immune to infection from outside, for at any time carriers from abroad may create carriers in Copenhagen, and they in their turn may convey the disease to susceptible persons.

In his note on this subject in *Ugeskrift for Læger* for Oct. 25, Dr. Bojlén compares the response to voluntary diphtheria vaccination with that to compulsory smallpox vaccination. In the school year 1950-1951, the percentage of children vaccinated against smallpox in the first six classes in the schools of Copenhagen was 98.9. Exemption from smallpox vaccination by a medical officer of health accounted for 0.5%, and postponement of smallpox vaccination accounted for another 0.5%. The unvaccinated represented only 0.1%; however, response to the invitation for voluntary vaccination against diphtheria has been almost as good and is an eloquent tribute to the principle of voluntary action.

LONDON

The Naming of Drugs.—The problem of naming drugs and the multiplicity of trade names has been reviewed in an address to the Pharmaceutical Society of Great Britain by Dr. F. Hartley, director of research of a leading pharmaceutical company in England. The total British income from the export of drugs and pharmaceuticals in 1951 was £31,000,000, of which proprietary-named products were responsible for £10,000,000. This represents 70% of their home sales value. In 1942 the British Pharmacopoeia Commission set up a nomenclature committee to recommend suitable names for adoption by the commission as approved names for new drugs, the understanding being that, should a drug ultimately be included in the British Pharmacopoeia, the approved name would be adopted as the official name. An unfortunate complication with regard to these names is that there have already been several examples of registration overseas by manufacturers in other countries who have used the same names. This has meant that British manufacturers have been unable to use these names in the countries concerned. Action by the Foreign C... been ineffecti... stopping this abuse, but inter... through the... Health

Organization may prove effective. In several countries registration of a name can be obtained only if it is already registered in Great Britain. Many countries require a certificate from the Ministry of Health that the product is known and used in Great Britain under the name that is to be used in the country overseas.

The problems involved in coining a name for a new drug are scarcely appreciated by the majority of physicians. First of all, the name must not clash with any name already on the trademarks register; then it must be distinctive and easy to remember, write, and pronounce. These last three requirements are often difficult to reconcile with one another. One way of aiding memory is to give the drug a name that gives an indication of its usage, i. e., "convey some anatomical, physiological, pathological or therapeutic suggestion." Several objections arise at once, however; such a name might have an adverse psychological effect on the patient, and, if there were more than one drug with the same therapeutic indications but with different potency or side-effects, confusion might arise and lead to disastrous results. It is for these reasons that the British Pharmacopoeia Commission recommends that approved names preferably be free from any such suggestions. On the other hand, there are instances in which this type of name may be of value, and there are already several such on official lists, e. g., ascorbic acid (vitamin C [implying antiscorbutic properties]), and testosterone (implying association with testicular tissue). Dr. Hartley considers that "the only feasible solution seems to be to form names by combining syllables from the scientific chemical names in such a way as to indicate something of the significant chemical groupings of the molecules." He states, "but if one then adds the provisions that the names must be distinctive in sound and spelling, easy to pronounce and remember and not liable to confusion with existing names, all within, say, not more than four syllables, the result may not always be pleasing to all!"

The use of initial letters is not considered "desirable for official description of the substance." Two recent examples of substances becoming well known by their initials and then being replaced by official names are BAL (British Anti-Lewisite), now known as dimercaprol injection (2,3-dimercaptopropanol), and DDT, now christened dicophane (chlorophenothane). Another possible method discussed was that of using capital letters, as in the case of the vitamins. It has been suggested, for instance, that the different antihistaminics might be known as antihist-A, antihist-B, and so on. The objections to this suggestion are that confusion would probably arise, because the antihistaminics, unlike the vitamins, all have the same action, and there are already similar registered names, e. g., antihist-A might be confused with "anthisan" (pyranisamine maleate).

A strong plea was made for close cooperation between the nomenclature authorities in different countries, as already exists between the British Pharmacopoeia Commission, the Council on Pharmacy and Chemistry of the American Medical Association, and the Scandinavian Pharmacopoeia Commission. Whenever possible, the name first selected in any one of the cooperating countries should be adopted. Dr. Hartley's final summing up was: "I think the essential factor influencing the naming of new drugs must be to continue to avoid conflict with registered names and to assist mental correlation of chosen names with the names for drugs of the same class of action. In general, therefore, approved names must continue, preferably, to be free from anatomical, pathological, physiological or therapeutic implications."

Osler's Last Illness.—At a recent meeting of the Osler Club, which was devoted to a symposium on pneumonia since Osler's time, Lord Horder gave an interesting account of Osler's last illness. On Dec. 12, 1919, Osler sent for Lord Horder to come to see him at Oxford. Lord Horder was shocked to find Osler very ill, intensely toxemic, and scarcely able to speak because of paroxysms of coughing. The history, the salient points of which had been jotted down in pencil by Osler, was that of a prolonged and obscure disease in the chest. Seven days previously, aspiration of the chest had produced a little serous fluid without any relief of symptoms. Lord Horder diagnosed an interlobar empyema; aspiration was repeated with as long a needle as could be obtained, and again a little serous fluid was obtained. A week later, the condition being unchanged, it was decided to aspirate again, and for the purpose two extra-long needles were made. The first aspiration was unsuccessful, but

by the second aspiration 4 to 5 ml. of foul pus was withdrawn. When the stylet was withdrawn from the needle on this second occasion, Osler remarked, "You've got it; my boy." The next day Charles Gordon-Watson drained an abscess cavity, but drainage was never copious and ceased three days later. A second operation failed to reveal any further pus. Death due to rupture of a blood vessel in the upper lobe of the lung claimed its victim with dramatic suddenness four days later.

New Development in Cataract Operations.—A preliminary report in *The Lancet*, by Mr. Harold Ridley, ophthalmic surgeon at St. Thomas' Hospital and Moorfields Hospital, on intraocular acrylic lenses for use after cataract operation has aroused much interest here. According to Mr. Ridley, it is now possible to substitute for the opaque crystalline lens an artificial intraocular lens capable of producing an excellent visual result. Such a lens can remain in an eye for at least two years without causing irritation. These conclusions are based on the results in 25 cases. The first two were unsatisfactory, owing to the fact that the experimental lens was too strong and produced myopia postoperatively. Of the other 23 cases, in only 1 was any difficulty encountered. Twenty-two were "all successful in that binocularly the visual result was better than it would have been with simple extraction alone." They were also "surgically satisfactory, having circular or nearly circular pupils, acrylic lenses in good position, normal tension, and no active iridocyclitis." Many patients see well without spectacles or with those they wore before the extraction. In one case two years have elapsed since the lens was introduced. The material of which the lens is made is "Trans pex 1," a variety of polymethyl methacrylate.

Mass Radiography Experiment.—An interesting experiment in preventive medicine is to be carried out in Islington, one of the more crowded and less salubrious suburbs of London. During the next 12 months, an attempt will be made to make roentgenograms of the chests of all adults living in the borough. For this purpose a new radiographic unit is to be opened, and booking offices will be established throughout the borough at which appointments for examination can be made. Mass radiograph examination, carried out since July, 1948, in the hospital region which includes Islington, has shown an incidence of tuberculosis of 2.2 per 1,000 persons examined. On the basis of these figures it is estimated that in Islington there are about 500 persons who have tuberculosis without being aware of it. By means of the total examination of the population it is hoped to track down these persons and thereby to reduce the spread of the infection.

MEXICO

Angiocardiographic Studies at the General Hospital, Mexico City.—In 1946, Dr. Alejandro Celis, chief of one of the neurological services at the General Hospital, Mexico City, and his co-workers Dr. Pacheco and Dr. del Castillo described a new method of angiocardiography. The procedure consists of the introduction of a Nélaton catheter through one of the external jugular veins, which, by way of the right atrium, reaches one of the branches of the inferior cava, or, passing from the atrium to the ventricle, arrives at the right or left pulmonary artery. Then a radiopaque substance is injected (40 cc. of iodopyrac concentrated solution, "nosylan"), and, after a certain length of time based on circulation time, one or more plates are exposed. This is done from the anteroposterior position if the pulmonary circulation is being studied and from a lateral position if the mediastinum is being studied.

The authors have utilized this method especially in differential diagnosis between mediastinal tumors and aneurysms in the mediastinum; this is made possible by the presence of the radiopaque substance in the lumen of the vessels. By the end of 1951, 300 cases had been studied, with excellent results. However, this method is contraindicated when endocarditis is present, because of the risk of embolism. In some cases it has been possible to visualize the upper hepatic veins, and in a case of the Cruveilhier-Baumgarten syndrome it was possible to visualize the porta. In recent months, Dr. Celis and his co-workers have been investigating the possibility of visualization of the thoracic duct using radiopaque material; so far, studies made with cadavers and animals have been encouraging.

CORRESPONDENCE

ESTABLISHMENT OF A GENERAL PRACTICE CLINIC

To the Editor:—The University of Tennessee, after a two-year study of the problem of general practice training, has inaugurated a program to give the general practitioner official status in the medical school and its teaching program. It is a typically American anomaly that, in medical education, the man who does nearly 85% of the medical practice in this country has absolutely no specific training for his job. In order to correct this it is proposed that the medical student devote a portion of his senior year to the general practice of medicine under the supervision of qualified general practitioners. The practice will be made to resemble, as nearly as possible, a typical, small-town general practice.

The general practice clinic has been set up as a part of the outpatient department of the hospital. The physical equipment will be made to resemble a typical, well-equipped small-town office. A 100 ma. x-ray, small laboratory, minor surgery, and physiotherapy room will be included in the clinic. X-ray and laboratory services will be performed under the direction of the students exactly as they are done in general practice.

Patients will be unselected and will be sent to the general practice clinic as they enter the outpatient department. No effort of any kind will be made to have the student see any particular type of case. Supervision will be largely by members of the Academy of General Practice from Memphis and surrounding towns. Under no circumstances will students observe the practice of medicine. Rather, they will do an active general practice with the advice and counsel of supervising physicians.

It is planned to place particular emphasis on the psychosomatic aspect of general practice. We feel that often a medical student may confuse a sociological work-up with the human understanding of a patient. This human understanding is a difficult matter to teach in a medical school. There is no scientific measurement of it, and there are no words with which to explain the quality to a student. It is hoped, however, that intimate contact with good general practitioners may serve to illustrate to the student this most necessary attribute of successful general practice.

Patient preference will be followed insofar as practical, and each student will be expected to see his own patients or to make arrangements for them to be seen by a colleague. In this manner we hope to allow the student to see the results of his own work and for him to assume to some degree the status of "family doctor" for the families who may be under his care.

Our contention is that general practice represents a coordination of knowledge gained in the specialty clinics, hospital wards, and lectures. We feel that nowhere in the medical curriculum has any effort been made to foster this coordination previously. We also feel most strongly that the average large outpatient department does not teach the proper approach to patients. Nor does it give good training for the myriad of personal problems of general practice.

It is hoped that the general practice clinics at the University of Tennessee will be the first step toward integrating general practice teaching with the rest of the medical school curriculum. Plans for the expansion of the sphere of the clinics are now under way; as general practice training proves its worth, more and more emphasis will be placed on this aspect of medical training.

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SOCIALIZED MEDICINE IN RUSSIA

To the Editor:—I have been working as a resident physician in the United States for only two years, but I have had bitter experience working as a physician in the Soviet Union for 17 years. I hope that my experience will be of some interest to my colleagues in the United States.

The primary unit of the Soviet Public Health Organization, the so-called polyclinic, in an average Soviet city is reserved for about 30,000 to 40,000 of the population. The area is divided into 10 to 15 districts, with 2,000 to 3,000 inhabitants living in each district. Such a district has its own physician and a nurse. Each patient seeking medical help and needing a certificate confirming his disease and justifying his sick leave must present himself to his district doctor or, if the patient is bedridden, must call his doctor to visit him at home. The patient does not have any choice of physicians, even if he has a preference. His district physician is appointed to remain his family doctor. Such a family doctor has three to three and a half office hours daily. The number of patients visiting him daily during his office hours is about 40 to 50, which means that about five minutes are allowed for each patient. After his office hours the doctor starts his calls, which amount to about 10 to 15 daily, or even 20 to 30 during epidemics.

Since he has no car and must walk, the Soviet district doctor needs at least three hours to make all his calls, and is able to stay in each home no more than about 10 minutes. During this time, he should perform the necessary physical examination and such procedures as the taking of the patient's temperature, blood pressure determination, writing of prescriptions, writing of sick leave certificates, and filling in the patient's chart.

The city hospitals are always overcrowded, with beds not only in sick rooms but also in the passages. All beds are theoretically distributed among polyclinics, but practically at least three days are needed to admit the patient to some hospital through the Central Bureau of Hospitalization, which regulates all the admissions.

In polyclinics there are also specialized divisions, such as tuberculosis, venereal disease, and prenatal care divisions. The tuberculosis division, for example, registers all tuberculosis cases and usually has hundreds and thousands of patients with acute pulmonary tuberculosis needing hospitalization. All beds in tuberculosis sanatoriums are, however, distributed among the trade unions, and admission to such a sanatorium depends more on the representatives of the trade unions in the factories than on the physician of the tuberculosis division. It sometimes happens that the trade union leaves an available bed in the tuberculosis sanatorium as a premium for an almost healthy worker, usually a "stachanowist," for use during his vacations.

The actually ill tuberculosis patient waits not just for many months but usually for several years, until his case becomes incurable. The time of a patient's stay in a tuberculosis sanatorium is limited to two months and can sometimes be prolonged by physicians for a maximum of two months. Consequently, the patient leaves the sanatorium still acutely ill and with positive sputum.

Before World War II, the average Soviet physician earned for his job in a hospital or polyclinic, if he had less than five years of practice, 300 rubles (\$75), if he had 5 to 10 years of practice, 350 rubles (\$87.50), and, if he had more than 10 years of practice, 400 rubles (\$100).

Let us remember that the real worth of such a salary in the years 1940 to 1951 corresponded to the price of one pair of shoes, while a suit cost 600 to 800 rubles (\$150 to \$200) and an overcoat 800 to 1,200 rubles (\$200 to \$300).

No Soviet doctor is prevented by law from having a private practice, provided he has enough space in his two room apartment. But the month after such a doctor starts such a "capitalist" business he will be taxed by authorities 10 times more than the amount of his entire income for the preceding time. Consequently, his business will be closed automatically.

In order to maintain his family the Soviet doctor is forced to have two jobs, working about 14 hours daily. In such a way the total income amounted before the last war to about 800 rubles, which was just enough to pay for an apartment and to have regular meals consisting mostly of bread, potatoes, vegetables, soups, and a little fat and meat. Buying of such things like a new suit, overcoat, or even shoes presented a very complicated problem for the Soviet doctor.

The Soviet Union has never published any statistics concerning the rates of morbidity and mortality; the only figure I can remember is for tuberculosis mortality, which, in the best times before the war, has never been less than 150 per 100,000 population. This is six times higher than the U. S. rate in 1949.

These are the achievements of the Soviet socialized medicine.

M.D.

INTERPRETATION OF CHEST X-RAY FILMS

To the Editor:—Your editorial "Reliability of Interpretation of Chest X-Ray Films," which appeared in THE JOURNAL Dec. 29, 1951 (147:1765) was most interesting. The high percentage of disagreements, up to 30%, by various physicians and 15% among the same doctors on the same films, at a later date, accounts for the fact that not a few persons receive tuberculosis care when the actual diagnosis may be allergic bronchial asthma, existing alone or concurrently with healed tuberculosis.

Over 25 years ago, at a medical school and large tuberculosis hospital, I called attention to a number of such cases diagnosed as active tuberculosis that really were allergic bronchial asthmas, alone or coexisting with inactive tuberculosis. Too much reliance was placed, as now, on the x-ray. In one patient who had coexisting active syphilis of the larynx with active pulmonary tuberculosis, the prognosis and result were completely changed recognition of the possibility of coexisting active disease
 gelsher, D. L.: Coexisting Active Syphilis of the Larynx with
 ive Pulmonary Tuberculosis, *J. A. M. A.* 89:284 [July 23]
 -7).

These x-ray errors parallel in frequency diagnoses made in the field of allergy when opinions are based on skin tests alone. Testing outfits are purchased with the belief that all allergy problems are automatically solved by these tests. This procedure alone is comparably erroneous. For example, although aspirin sensitivity will not produce a positive skin test, the experienced allergist can diagnose this sensitivity by history and observation. On the other hand, many patients with positive skin tests have no clinical manifestations.

These facts emphasize the importance of not depending solely on chest x-ray shadows in the diagnosis of tuberculosis. Such a procedure must be coupled with further study.

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FOREIGN BODY IN THE NOSE

To the Editor:—The report on "Angioneurotic Edema Due to Foreign Body Long Present in the Nose" (*J. A. M. A.* 147:1234 [Nov. 24] 1951) interested me because it raises controversial questions, which may be summarized as follows:

1. As to the etiology of the angioneurotic edema, if it is true that a peanut imbedded in the nose could lead to angioneurotic edema of the eyelids, then how is one to explain the "strongly fetid" local area in the nose as an allergic focus? More likely, one would think of a localized infection rather than an allergy. No mention is made of skin tests made with peanut extract to

induce an urticarial skin reaction to prove an allergic involvement of the eyelids, legs, lips, forehead, and wrist.

2. As to the nature of the angioneurotic edema, no mention is made as to whether the eyelid edema was greater on the side of the nose in which the peanut was lodged or whether there was cellulitis or tenderness over the cheek on that side. The author states that the patient "had awakened every morning with a swelling of the face that usually receded during the day." That would suggest a postural factor in this edema. Furthermore, unlike the patient with angioneurotic edema, this patient had only "light headaches" and had "suffered from very frequent colds," which again suggests a nose infection rather than an allergic edema.

The significant and gratifying feature in this case is that an edema affecting different parts of the body, and apparently postural in nature, disappeared after a fetid peanut was removed from the nose. There is no proof that we are dealing with an allergy. Nor is the diagnosis of angioneurotic edema of the eyelids established. No mention is made of skin tests or of blood tests to exclude eosinophilia or of epinephrine injection to counteract the edema. Stress is laid on nose findings, but there is no eye report, which would include vision, possible edema of the optic nerve head, allergic exophthalmos, or restriction in eye movements as a result of the edema. I wonder whether in the absence of more complete data one is justified in employing the term "angioneurotic edema."

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INTERNATIONAL SOCIETY OF AEROSOLOGY

To the Editor:—I would appreciate the publication of this letter, calling the attention of physicians who are particularly interested in aerosol therapy to a brief review of the meetings on aerosol therapy held in Turin, Italy, on June 1 and 2, 1951, which appeared in the News and Notes section of *Science* (Prigal, S. J.: Italian Congress on Aerosol Therapy) 114:561 (Nov. 23) 1951.

At the conclusion of these meetings it was decided to organize an International Society of Aerosology, and I was elected to represent the United States. I invite correspondence from physicians, physicists, and others who are interested in this new field, in order to judge whether there is sufficient interest for the formation of an American branch of this society.

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HORSE SHOE CLUB

To the Editor:—It may interest any prospective medical visitors to Great Britain to know of the Horse Shoe Club. This club, which was founded in 1932, has the object of fostering Anglo-American relations in the medical field. It is particularly interested in aiding medical exchanges and in helping any visiting American to contact those who work in his own specialty. It also has certain funds that are devoted to providing entertainment for these visitors during their stay in Great Britain.

Inquiries should be addressed to the Honorary Secretary, Dr. C. S. Nicol, St. Bartholomew's Hospital, London, E.C.1, England.

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GIFT FOR AMERICAN MEDICAL DIRECTORY

To the Editor:—A few months ago, I noticed that the publication of the American Medical Directory had a small debt. I am sending a small check to help defray this amount. This directory, I think, is one of our most valuable tools.

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COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

RESIDENCY INFORMATION SERVICE

A list of residencies in approved hospitals in which positions are presently open is now ready for distribution and will be furnished to physicians on request. The Residency Information Service list, first announced in *THE JOURNAL*, April 21, 1951, was to have been revised monthly. Experience has shown, however, that it is impracticable and unnecessary to revise the list on a monthly basis. In the future, the list will be published periodically. Prior to publication, all hospitals conducting approved programs will be circularized for a list of current vacancies.

These lists provide information regarding the number of positions open, date available, the name of the chief of service, the stipend paid, maintenance furnished, and the name of the person to whom application should be made; in addition, the lists indicate those hospitals that will consider applications from graduates of medical schools located outside the United States.

It should be noted that this service is made available directly to prospective applicants on their request and is not published in *THE JOURNAL*. Complete data on all approved services will continue to be published in the Internship and Residency Number of *THE JOURNAL*.

Communications regarding this service, from either hospitals or physicians, should be addressed to: Residency Information Service, Council on Medical Education and Hospitals, 535 North Dearborn St., Chicago 10.

COUNCIL ON MEDICAL SERVICE

AID GIVEN TO MEDICAL ESSAYISTS

When the Council on Medical Service was established in 1943, one of the functions outlined for it by the House of Delegates was "To make available facts, data, and medical opinions, with respect to timely and adequate rendition of medical care to the American people."¹ The Council has complied with this directive by distributing upon request such material as is available on the nonscientific aspects of the practice of medicine.

Among the topics concerning which many requests are received is the proposed national compulsory health insurance program. Interest in this topic was stimulated as early as 1935-1936, when the National University Extension Association chose as the official debate proposition, "RESOLVED: That the Several States Should Enact Legislation Providing for a System of Complete Medical Service Available to All Citizens at Public Expense." During the next few years interest in the subject was sporadic, gaining little headway nationally. However, the so-called Wagner-Murray-Dingell bills of 1943, 1945, and 1947 gave considerable impetus to and aroused nationwide interest in health insurance, to the degree that during the 1946-1947 school year, the N.U.E.A. selected as its debate topic, "RESOLVED: That the Federal Government Should Provide a System of Complete Medical Care Available to All Citizens at Public Expense." On the request for authentic information by the National University Extension Association, representing approximately 7,500 schools, the Council on Medical Service prepared a compilation of 35 articles, entitled "Voluntary Health Insurance vs. Compulsory Sickness Insurance," to be used by the debaters. From this date on, health insurance, socialized medicine, and medical care have figured, in one way or another, in debate and essay topics throughout the nation. As the demands for factual reference material increased, the Council prepared additional data, procured other informative literature, and distributed it to schools and individuals on request. To be convinced of the widespread interest in this general subject one has only to recall

that requests received during 1946 and 1947 required only about 20,000 pieces of material, but since 1947 the total has increased steadily, and now is well over 150,000 pieces annually.

The National Forensic League and the National High School Debate Society, during the 1950-1951 season, chose as their official proposition, "RESOLVED: The American People Should Reject the Welfare State." To assist students throughout the country, the Council compiled 15 of the most pertinent articles into one brochure entitled, "Medicine and the Welfare State." More than 5,000 copies of this booklet were distributed on request during the first three months after its publication, and it was necessary to have two additional printings made within the first year.

The Woman's Auxiliary to the American Medical Association has, in the past years, encouraged its constituent state and component county auxiliaries to promote or sponsor local essay contests and debates. To assist these groups, the Council on Medical Service, in September 1950, prepared an instruction leaflet, entitled "Suggested Rules for School Essay Contests." The leaflet covered essentially the following points: eligibility, contest committees, suggested titles, sources of reference material, form and length of essay, time limits, awards, judging, and hints for running a contest successfully. Essay contests of this type, for which the Council supplied reference material, have been sponsored by either state or local auxiliary groups in such states as California, Florida, Kansas, Kentucky, Louisiana, Missouri, Ohio, Pennsylvania, and Tennessee. The essay subject material covered a broad range. Some of the titles used were: "The Role of Medicine in Preserving the American Way of Life," "Fifty Years of Medical Progress," "Voluntary or Compulsory Health Insurance, Which Shall It Be?," and "The Growth of Voluntary Health Insurance in the United States." Branches of service clubs, such as The American Legion, Rotary, and Kiwanis, have also promoted this type of activity, as have several of the medical specialty societies.

One of the larger and better known competitions is the annual \$1,000 essay contest, which is open to students of the 7th through the 12th grades and which is sponsored by the Association of American Physicians and Surgeons. The series started in 1946 and has had the permanent subject, "Why the Private Practice of Medicine Furnishes This Country with the Finest Medical Care." Many medical societies and auxiliaries co-sponsor this contest locally, adding supplemental prizes for area contestants. The Council on Medical Service initially assisted this association by supplying kits of reference material. During the past two years the A. A. P. S. prepared its own kits, and the Council supplied articles and reprints for inclusion. During the 1949-1950 contest, the Council supplied more than 8,050 pieces of literature for inclusion in the A. A. P. S. kits, exclusive of the reference material sent by the Council directly to participating students in response to their individual requests. During the 1950-1951 contest, more than 7,550 articles and pamphlets, including "Medicine and the Welfare State," were included in the A. A. P. S. kits. For the 1951-1952 A. A. P. S. contest, more than 35,000 items have already been made available by the Council for the essay kits.

The Council has made a practice of distributing literature only upon request; however, in order to serve more fully the needs of students, teachers, librarians, and other interested persons, the Council has prepared, and revises periodically, a check-list of reference material, which is available through its office. In this manner a minimum of material can be sent, and, at the same time, the recipient is apprised of additional material available. A bibliography of articles on health insurance, medical care, and the welfare state, which have appeared in national magazines, and listings of books on these topics are also available upon request. Some of the more frequently requested Council publications have been listed in "Educator's Guide to Free Material," published by Educators Progress Service, and the H. W. Wilson Company's "Vertical File Service Catalog" for librarians. By these means large numbers as well as a great variety of publications are now found in high school, college, and public libraries.

1. Council on Medical Service and Public Relations—The Purposes and Functions of the Council, J. A. M. A. 123:914 (Dec. 4) 1943.

BUREAU OF LEGAL MEDICINE AND LEGISLATION

MEDICOLEGAL ABSTRACTS

Privileged Communications: Physician-Patient Relationship; Attorney-Client Relationship.—The plaintiff filed suit for damages for personal injuries against the City and County of San Francisco and the Western Pacific Railroad Company. From an adverse ruling in the trial court, the defendants filed an original mandamus action in the Supreme Court of California.

At the trial, the plaintiff alleged that he suffered brain concussion, nerve root damage and nervous shock as a result of the injuries which he received. At the request of the plaintiff's attorneys, Dr. Catton, a physician specializing in nervous and mental diseases, twice gave the plaintiff a neurological and psychiatric examination. In his deposition, Dr. Catton testified that there was no physician-patient relationship between him and the plaintiff; that he did not advise or treat the plaintiff; that the sole purpose of the examination was to aid the plaintiff's attorneys in the preparation of a lawsuit for the plaintiff; and that he was the agent of the attorneys. He refused to answer questions concerning the plaintiff's condition on the ground that the information sought was privileged under the law relating to the physician-patient privilege, under the law relating to the attorney-client privilege and also for the reason that "the use of faculties of a physician, neurologist, and psychiatrist and for an opinion based thereon, which opinion is a part of my property which I do not wish to be deprived of without due compensation and arrangements having been made in relation thereto" authorized such refusal.

The California statute provides that "a licensed physician or surgeon can not, without the consent of his patient, be examined in a civil action, as to any information acquired in attending the patient, which was necessary to enable him to prescribe or act for the patient." Under the circumstances of this case, said the Supreme Court, there is no physician-patient privilege. That privilege can not be invoked when no treatment is contemplated when. If the person examined is not a patient, there is no physician-patient relationship and therefore no physician-patient privilege. Even if there had been a physician-patient relationship, the Supreme Court continued, the privilege would be waived in this case by the plaintiff's bringing the action for personal injuries. The whole purpose of the privilege is to preclude the humiliation of the patient that might follow disclosure of his ailments. When the patient himself discloses those ailments by bringing an action in which they are in issue, there is no longer any reason for the privilege. The patient-litigant exception precludes one who has placed in issue his physical condition from invoking the privilege on the ground that disclosure of his condition would cause him humiliation. He can not have his cake and eat it too.

Dr. Catton also asserted a privilege personal to himself, a privilege not to testify to knowledge and opinions that were the result of his special learning without payment of more than the ordinary witness fee. The defendant asked him to testify, not by reason of his expertness in a special field, but because of his knowledge of specific facts as to the plaintiff's condition, facts pertinent to an issue to be tried. He is like any other witness with knowledge of such facts; it is immaterial that he discovered them by reason of his special training. In testifying as a witness he would simply be imparting information relevant to the issue, as he would had he been a witness to the accident in which the plaintiff was injured. A physician who has acquired knowledge of a patient or of specific facts in connection with a patient, may be called upon to testify to those facts without any compensa-

tion other than the ordinary witness receives for attendance upon court.

The Supreme Court held, however, that the plaintiff was permitted to invoke the attorney-client privilege in this case. The statutes in regard to the attorney-client privilege provide "An attorney can not, without the consent of his client, be examined as to any communication made by the client to him, or his advice given thereon in the course of professional employment; nor can an attorney's secretary, stenographer, or clerk be examined, without the consent of his employer, concerning any fact of the knowledge of which has been acquired in such capacity." The defendant contended that under the terms of this statute, it is only the attorney and the attorney's secretary, stenographer or clerk who cannot be examined and that since Dr. Catton was not engaged in any of these capacities, he cannot withhold the information requested. The statute specifically extends the client's privilege to preclude examination of the attorney's secretary, stenographer, or clerk regarding information of communications between attorney and client acquired in such capacities, to rule out the possibility of their coming within the general rule that the privilege does not preclude the examination of a third person who overhears or otherwise has knowledge of communications between a client and his attorney. It does not follow, however, that intermediate agents of communication between attorney and client fall within that general rule. Had the plaintiff himself described his condition to his attorneys there could be no doubt that the communication would be privileged and that neither the attorney nor the plaintiff could be compelled to reveal it, even though a client is not listed in the statute among those who cannot be examined. It is no less the client's communication to the attorney when it is given by the client to an agent for transmission to the attorney, and it is immaterial whether the agent is the agent of the attorney, the client, or both. The client's freedom of communication requires a liberty of employing other means than his own personal action. The privilege of confidence would be a vain one unless its exercise could be thus delegated. A communication, then, by any form of agency employed or set in motion by the client is within the privilege. Thus, when communication by a client to his attorney regarding his physical or mental condition requires the assistance of a physician to interpret the client's condition to the attorney, the client may submit to an examination by the physician without fear that the latter will be compelled to reveal the information disclosed. The defendant contended, however, that the purpose of the patient-litigant exception would be defeated if the attorney-client privilege in the statute can be invoked to prevent a physician from divulging the results of his examination of a person for the purpose of aiding his attorneys in the preparation of an action for personal injuries. The two subdivisions, said the Supreme Court, relate to two separate and distinct privileges. It does not follow that if there is no physician-patient privilege there can be no attorney-client privilege. The patient-litigant exception applies only to the physician-patient privilege and there is no corresponding client-litigant exception. Had Dr. Catton treated the plaintiff before being asked to serve as an intermediate agent between the plaintiff and his attorneys the patient-litigant exception would apply and Dr. Catton would then have been like any other witness with knowledge of facts pertinent to an issue to be tried. The exception could not be defeated by asking the physician to reveal his knowledge of the facts to the attorneys, for a litigant cannot silence a witness by having him reveal his knowledge to the litigant's attorney. Similarly, if Dr. Catton should now treat the plaintiff, any information acquired in the course of that treatment would not be privileged, although the results of his previous examination and his reports to the plaintiff's attorneys would be.

Accordingly the writ of mandamus requesting that Dr. Catton be ordered to answer the questions propounded to him at the trial of the case was discharged.—*City and County of San Francisco v. Superior Court*, 231 P. (2d) 26 (California, 1951)

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Arch. Indust. Hyg. & Occup. Med., Chicago

4:417-518 (Nov.) 1951

- Treatment of Cyanide Poisoning in Industry. J. H. Wolfscie.—p. 417.
 Space- and Labor-Saving Devices in Industrial Dispensary: IV. Clinical-Record Distribution Box for Physician's Office. J. S. Felton.—p. 426.
 Id.: V. Optical Dispensing Unit. J. S. Felton.—p. 432.
 Id.: VI. Multipurpose Central Clerical Desk for Treatment Room. J. S. Felton.—p. 437.
 X-Ray Diffraction Study of Sputum in Silicosis. F. Meyer and S. Solomon.—p. 443.
 Characteristics of Suction Soap Film Meter: Suctionometer—New Low-Velocity-Measuring Device. B. D. Bloomfield and L. Silverman.—p. 446.
 Preliminary Observations on Toxicity of Elemental Selenium. R. H. Hall, S. Laskin, P. Frank and others.—p. 458.
 Response of Rodents to Repeated Inhalation of Vapors of Tetraethyl Orthosilicate. U. C. Pozzani and C. P. Carpenter.—p. 465.
 Vapor Toxicity of Trichloroethylene Determined by Experiments on Laboratory Animals. E. M. Adams, H. C. Spencer, V. K. Rowe and others.—p. 469.
 Vapor Toxicity of Ethylene Dichloride Determined by Experiments on Laboratory Animals. H. C. Spencer, V. K. Rowe, E. M. Adams and others.—p. 482.
 Toxicity of Imidazoline (or Glyoxalidine) Fungicide. C. P. Carpenter, C. S. Weil and H. F. Smyth Jr.—p. 494.

A.M.A. Arch. Ophthalmology, Chicago

46:477-600 (Nov.) 1951

- Competitive Action of Miotics on Iris Sphincter. K. C. Swan and L. Gehrsitz.—p. 477.
 Studies of Corneal Transparency Under Various Experimental Conditions. K. van Walbeek and H. Neuman.—p. 482.
 *Micro-Organisms Causing Sympathetic Ophthalmia. E. Schreck.—p. 489.
 Localization of Lacrimal Sac in Dacryocystorhinostomy by Transillumination. L. Christensen.—p. 501.
 Gonioscopic Study of Fistulizing Operations. A. G. DeVoe.—p. 504.
 Uveitis, Poliosis, and Alopecia in Siblings: Case Report. W. H. Benedict and W. L. Benedict.—p. 510.
 *Methods for Early Diagnosis of Multiple Sclerosis: Observations with Special Reference to So-Called Ocular Type. O. Lowenstein.—p. 513.
 Corneal Dystrophy Following Secondary Intraocular Operations. P. Sternberg and S. J. Meyer.—p. 527.
 Band Keratopathy in Disturbances of Calcium Metabolism. G. W. Ojers and J. Alfano.—p. 531.
 Studies on Crystalline Lens: IV. Distribution of Cytochrome, Total Riboflavin, Lactate, and Pyruvate and Their Metabolic Significance. V. E. Kinsey and C. E. Frohman.—p. 536.
 Experiment in Which 50 Presbyopes Were Provided with Trifocal Glasses. P. W. Miles.—p. 542.
 Adrenergic Blocking Agents in Treatment of Glaucoma. C. R. Mullen and I. H. Leopold.—p. 549.
 Unilateral Proptosis Due to Fibrous Dysplasia of Bone: Report of Two Cases. R. B. King and G. J. Hayes.—p. 553.
 Localized Injection of Upper Quadrant of Bulbar Conjunctiva. A. deRoeth Sr.—p. 560.
 Description of an Ophthalmoscope for Examining Retina in Living Eye. H. von Helmholtz.—p. 565.
 Acute Glaucoma Simulating Acute Iritis. M. Posner.—p. 584.
 Neuro-Ophthalmology. C. W. Rucker.—p. 586.

Micro-Organisms Causing Sympathetic Ophthalmia.—By introducing material from patients with sympathetic ophthalmia into the eyes of chickens, Schreck reproduced the histopathological picture of sympathetic ophthalmia. The process was continuous,

starting from the exciting eye and traveling over the chiasm to the sympathizing eye. The author also demonstrated that micro-organisms causing sympathetic ophthalmia could be grown on the chorioallantois of the chick embryo. As human donor material, the aqueous of exciting eyes was used twice, the aqueous of sympathizing eyes, seven times, and uveal material from exciting eyes, three times. On the basis of these experiments and a review of the histological preparations made in 54 published cases of sympathetic ophthalmia, the author postulated that the exciting agent of sympathetic ophthalmia remains as a saprophytic, harmless parasite in the conjunctival sac, in its epithelial cells, in the adventitial cells of the conjunctival and episcleral vessels, in the vessels of the limbal arcade, and in the endothelial cells of Tenon's capsule. Only when the micro-organism comes in contact with uveal tissue does it become virulent and pathogenic. This can happen whenever the corneoscleral barrier is opened, e. g., by a perforating injury, operation, or tumor, when the uveal tissue becomes exposed. Inoculation of the lens with the organism causes Type I, sympathetic ophthalmia, with anterior uveitis and migrating periangiitis of the retina and the optic nerve. Invasion of the infective agent into the exposed uveal tract produces Type II, sympathetic ophthalmia, with anterior and posterior uveitis and migration of the pathogen as periangiitis and perineuritis along the ciliary nerves and the optic nerve. In view of the general experience with the Rickettsia group of organisms, to which the exciting agent of sympathetic ophthalmia seems to be related, not much help can be expected from the sulfonamides, penicillin, or streptomycin. It would seem worth while, however, to try aureomycin, chloramphenicol, *p*-aminobenzoic acid and *p*-aminosalicylic acid. The old proved methods such as early enucleation of the suspected eye, not evisceration of the eyeball, and treatment with methenamine sodium salicylate remain helpful.

Early Diagnosis of Multiple Sclerosis.—Multiple sclerosis is characterized by the occurrence of scattered demyelinated patches in the white matter throughout the central nervous system. Both sensory and motor pathways are involved, and the neurological symptoms vary greatly, according to the location of the lesions. It is not at all necessary for diagnosis that the symptoms due to demyelinating lesions be situated far apart; it is essential only that they are located in different neurons, and that they are not caused by a single though extensive process, such as an inflammation or tumor. Since it is important to discover the early, minute, or latent symptoms, and thereby demonstrate the presence of multiple lesions, special methods of investigation may be needed. The author describes diagnostic methods not previously reported in the literature. He shows how a diagnosis can be established (1) when ocular symptoms due only to one lesion suggest multiple sclerosis, and the usual neurological examination reveals no abnormality; or (2) when neurological symptoms outside the visual apparatus, due only to one lesion, are suggestive of multiple sclerosis, and the usual ophthalmologic methods (examination of fundus, visual fields, and extraocular muscles) yield no evidence of a lesion. He describes methods and apparatus for detection of low-degree paresis, latent tremor of the head or extremities, differences of muscle tonus between the right and left extremities, and nystagmus. When symptoms outside the visual apparatus are insufficient to establish a diagnosis of multiple lesions, and ophthalmological examination shows no abnormality, pupillography may reveal hidden symptoms that point to the presence of lesions in additional neurons, thereby making the diagnosis possible early. Patients with two or more attacks of the disease usually show both ocular (including pupillary) and general symptoms.

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Titles marked with an asterisk (*) are abstracted.

Alabama State Medical Assn. Journal, Montgomery

21:109-148 (Nov.) 1951

- Cor Pulmonale. J. C. Nash.—p. 109.
 Acute Myocardial Infarction: Review of Clinical Course and Management of 90 Cases. E. D. Lineberry, O. C. McCarn and W. H. Kessler.—p. 114.
 Early Use of Mercurial Diuretics in Myocardial Infarction. W. J. Atkinson Jr. and G. O. Segrest.—p. 118.
 Heart Disease in Pregnancy. J. C. Carmichael, S. Goodman and C. C. Blanton.—p. 121.
 Acute Benign Non-Specific Pericarditis. T. E. Bridges and C. E. Porter.—p. 124.
 Patent Ductus Arteriosus. W. A. Clyde and C. J. Donald.—p. 129.

American Heart Journal, St. Louis

42:643-800 (Nov.) 1951

- *Disturbances in Cardiac Mechanism of Several Hours' Duration Complicating Cardiac Venous Catheterization. N. O. Fowler, R. N. Westcott and R. C. Scott.—p. 652.
 *Myocardial Damage Following Inadvertent Deep Cannulation of Coronary Sinus During Right Heart Catheterization. W. W. Smith, R. E. Albert and B. Rader.—p. 661.
 Obstructing Left Auricular Thrombi. G. Miller, B. L. Stolzer and M. Zuckerbrod.—p. 667.
 Serum Electrolytes and Electrocardiogram. T. B. Reynolds, H. E. Martin and R. E. Homann.—p. 671.
 Extracardiac Arteriovenous Fistulas in Thorax. E. J. Marchand, M. R. Hejtmanick and G. R. Herrmann.—p. 682.
 *Use of Carboxylic Cation Exchange Resin in Therapy of Congestive Heart Failure. A. W. Feinberg and B. Rosenberg.—p. 698.
 Method for Objective Evaluation of Physical and Drug Therapy in Rehabilitation of the Hemiplegic Patient. S. H. Rinzler, H. Brown and J. G. Benton.—p. 710.
 Objective Evaluation of Physical and Drug Therapy in Rehabilitation of the Hemiplegic Patient: I. Study of Dihydroergocornine (DHO-180). J. G. Benton, H. Brown and S. H. Rinzler.—p. 719.
 Case of Heart Block Treated with 1-Cyclohexyl-2-Methylaminopropane (Benzedrex). J. Day and W. N. Viar.—p. 733.
 Tuberculous Pericarditis: Study of 41 Cases with Special Reference to Prognosis. J. A. Wood.—p. 737.
 Use of Vinyl Plastic Tubing in Recording Pressure Phenomena. D. B. Arst, M. Silver and W. J. Lahey.—p. 746.

Complications of Cardiac Catheterization.—Disturbances in cardiac mechanism that persisted following withdrawal of the catheter developed in 9 of 106 patients on whom 110 venous catheterizations of the right side of the heart were performed. These disturbances consisted of right bundle branch block in seven patients, auricular fibrillation in one, and frequent ventricular premature contractions in another. Follow-up electrocardiograms were made in eight of the nine patients, and the rhythmia disappeared within 12 hours. In these instances, rhythmia developed as often in normal as in diseased hearts. Although spontaneous recovery took place in the authors' cases, three fatal arrhythmias were described in the literature and more have undoubtedly occurred. If the arrhythmias following catheterization of the heart are not fatal, they usually disappear within 12 hours, but it should be emphasized again that catheterization of the human heart is not a procedure to be undertaken lightly. Constant fluoroscopic and direct-writing electrocardiographic observations are believed essential to the procedure.

Myocardial Damage in Cardiac Catheterization.—Cardiac catheterization was done in a man, 61, with mild pulmonary emphysema associated with anorexia and weight loss but without clinical and roentgenologic evidence of cardiovascular disease. The patient then received injections of 10 mg. of desoxycorticosterone acetate intramuscularly daily, with supplementary sodium chloride by mouth. After 25 days, he had gained 11 lb. (5 kg.) and minimal ankle edema had developed. Hemodynamic studies then were repeated and clinical evidence of myocardial damage developed following cardiac catheterization, in the process of which the catheter had inadvertently been advanced deeply into the coronary venous tree for several minutes. Electrocardiographic changes developed immediately on introduction of the catheter and subsequently assumed the configuration characteristic of pericarditis. That this is not an isolated, rare event is illustrated by reference to several cases reported by British authors. All patients survived. It is probable that catheterization of the coronary venous system is dangerous only if the catheter has a relatively large outside diameter and is inserted deeply. Several investigators have shown that inserting the catheter tip only a short distance into the coronary sinus may be done safely, and there is evidence that the coronary

venous tree will tolerate a small catheter even if inserted deeply. It is therefore suggested that great care be taken in catheterizing the right ventricle and that the course of the catheter be checked by fluoroscopy in the right oblique position and by observing the pattern of the pressure tracing from the catheter tip immediately after it has appeared to traverse the tricuspid valve.

Cation-Exchange Resin in Congestive Heart Failure.—Ion exchangers are insoluble substances, natural or synthetic, which remove one ion from solution in exchange for another. Cation exchangers remove sodium, potassium, and calcium ions from solution. Most cation exchangers in clinical use are synthetic resins. A carboxylic acid cation exchange resin, containing a mixture of the ammonium and potassium forms, was administered to six patients with chronic congestive heart failure and to one patient with the nephrotic syndrome for periods ranging from six weeks to one year, most of the time on an outpatient basis. Between 30 and 60 gm. of resin a day was given in divided doses with meals. Five of the six cardiac patients were benefited by the treatment to the extent that there was a pronounced reduction in the number of mercurial injections necessary to keep them symptom free. The sixth cardiac patient, who had impairment of renal function, had a toxic reaction in the form of uncompensated acidosis. He also developed hypokalemia with evidences of digitalis intoxication. One patient had an episode of salt depletion during unusually hot weather. Diuresis was not induced in the nephrotic patient by treatment with this resin. The use of this resin appears to be practical for the treatment of ambulatory patients with cardiac failure who can be followed closely. A carbon dioxide combining power above 20 mEq. per liter appears to be a safe level. The resin should be used with extreme caution in patients with inadequate kidney function.

Am. Journal of Obstetrics and Gynecology, St. Louis

62:713-942 (Oct.) 1951.

- Etiology of Uterine Flexures, with Proper Mode of Treatment Indicated. T. A. Emmet.—p. 713.
 Extirpation of Functionally Active Ovaries for Remedy of Otherwise Incurable Diseases. R. Battey.—p. 718.
 Labor Complicated by Uterine Fibroids and Placenta Previa. J. Chadwick.—p. 722.
 Latent Gonorrhea, Especially with Regard to Its Influence on Fertility in Women. E. Noeggerath.—p. 726.
 Presidential Address. Adventure at Avernus. F. C. Irving.—p. 732.
 Enterocoele. C. D. Read.—p. 743.
 Experience with Rh Factor in 1,000 Consecutive White Obstetrical Patients. E. L. King and J. A. King.—p. 758.
 Studies of Blood Oxygen Saturation and Causes of Death in Premature Infants. E. S. Taylor, W. C. Scott and C. D. Govan.—p. 764.
 Paget's Disease of the Vulva. C. P. Huber, S. H. Gardiner and A. Michael.—p. 778.
 Bacteriologic and Clinical Study of Pyometra. B. Carter, C. P. Jones, R. A. Ross and W. L. Thomas.—p. 793.
 Clinical Considerations of Benign Ovarian Cystomas. C. L. Randall and D. W. Hall.—p. 806.
 Malignancy of Special Ovarian Tumors. D. N. Henderson.—p. 816.
 Excretion and Concentration of Urine Solutes During Normal Pregnancy as Measured by Freezing Point Depression. W. L. Caton, D. E. Reid and C. C. Roby.—p. 827.
 Complete Cesarean Hysterectomy. M. E. David.—p. 838.
 *Radical Hysterectomy with Bilateral Pelvic Lymph Node Dissections: Report of 100 Patients Operated on Five or More Years Ago. J. V. Meigs.—p. 854.
 *Effect of Radiation on Metastatic Pelvic Lymph Node Involvement in Carcinoma of the Cervix. W. E. Brown, I. Meschan, E. Kerekes and J. M. Sadler.—p. 871.
 Prevention of Thrombosis and Embolism in Gynecological Surgery. J. P. Pratt, C. P. Hodgkinson and F. G. McConnell.—p. 890.
 Nutritional Deficiencies as a Causal Factor in Toxemia and Premature Labor. W. T. Tompkins and D. G. Wiesel.—p. 898.
 Ovarian Pregnancy. L. Gerin-Lajolle.—p. 920.
 Clinical and Surgical Review of Endometriosis. V. S. Counsellor and J. L. Crenshaw Jr.—p. 930.

Surgical Treatment of Carcinoma of Cervix.—Although irradiation is widely accepted as the proper treatment for carcinoma of the cervix, Meigs believes that competently performed surgery without radiation has a definite place in the treatment of this disease. He bases his opinion on the results of a five-year follow-up study of 85 patients treated by radical hysterectomy with bilateral pelvic lymph node dissections. Surgical therapy was undertaken because of the frequent recurrences after irradiation, the radioresistance of some tumors, the failure of irradiation to eradicate metastatic cancer in the pelvic lymph nodes, and the

bowel injury frequently resulting. Patients were selected for operation solely on the basis of their physical condition and not the extent of the cancer. Most of them had cancers in stages 1 or 2 although some were in stages 3 or 4. Patients with intra-epithelial cancer were excluded. At operation the common iliac, external, and internal iliac, ureteral, obturator, and presacral nodes were removed along with as much paracervical, paravaginal, and pararectal tissue as possible. Cancer cells were found in the nodes of 22.4% of the patients. There were no operative deaths. The five-year survival rate was 74.1% for the entire group of 85 patients and 26.3% for those with lymph node metastases. Postoperative complications included ureterovaginal fistulas in 7.2% of the patients and disturbances of bladder function in most patients. The addition of radiation therapy did not decrease the incidence of node involvement nor increase the survival rate or the incidence of fistulas. Meigs concludes that there is no indication for combined irradiation and surgical therapy, and that irradiation should be reserved for those patients whose general condition does not permit surgical intervention. If in the future radioresistance of tumors can be predicted, this will also help in selection of the proper method of therapy.

Irradiation of Pelvic Lymph Nodes in Carcinoma of Cervix.—

According to Brown and co-workers, neither lymphadenectomy nor radiation therapy as currently practiced satisfactorily eradicates metastatic carcinoma of the pelvic lymph nodes arising from carcinoma of the cervix. To obtain further knowledge of the effectiveness of irradiation of these nodes, the authors delivered controlled amounts of x- and gamma-rays to the cervix and pelvic lymph nodes of 24 patients with carcinoma of the cervix and subsequently studied the nodes microscopically. X-rays were given through six to eight portals employing the factors 220 kv., 15 ma., target-skin distance 50 cm., and HVL 1.5 mm. Cu. Gamma roentgens were obtained from radium or cobalt 60 shielded by 1.0 mm. of platinum. An Ernst applicator or multiple needles were used as required. Combined gamma and x-ray roentgen doses totaled 5,000 to 6,000 r to the lateral pelvic wall, 10,000 r or more to the cervix, and less than 4,000 r to the rectum and bladder. The authors used the converted Quimby tables to calculate the tissue dose delivered to various points in the pelvis. From 2 to 12 months after irradiation the uterus and pelvic nodes were removed surgically and examined microscopically. In 18 of the 24 patients no residual carcinoma was found at operation in the cervix, pelvic lymph nodes, or parametrial tissue. In three patients there was residual carcinoma in the upper pelvis, presumably due to the fact that the iliac and subaortic nodes were at the edge of the field of x-irradiation where the dose was too small to be effective. The remaining three patients had residual carcinoma of the cervix and pelvis, which had proved resistant to 10,000 to 20,000 r. Postirradiation vesicovaginal fistulas developed in two patients. The authors conclude that a minimum of 5,000 to 6,000 tissue r delivered in five to six weeks is necessary to eradicate radiosensitive carcinoma in the pelvic lymph nodes. This amount can be given with minimal risk to normal viscera if several routes and modes of radiation therapy are combined. Radioresistant tumors may tolerate two to three times the usual cancerocidal dose of roentgens. If surgery is employed after irradiation, it should be done within two to three months before collateral circulation is seriously compromised.

American Journal of Orthopsychiatry, New York

21:667-888 (Oct.) 1951. Partial Index

- Psychiatry and the Child Health Services. L. Baumgartner.—p. 693.
- Mental Hygiene as Public Health Practice. R. H. Felix.—p. 707.
- *Mirth Response Test: Preliminary Report on Psychodiagnostic Technique Utilizing Dynamics of Humor. F. C. Redlich, J. Levine and T. P. Sohler.—p. 717.
- Psychoanalytic Study of Fraternal Twin. B. Karpman.—p. 735.
- Factors Influencing Adaptations of Organically Handicapped Children. V. E. Carter and S. Chess.—p. 827.
- Personality Structure and Therapeutic Manipulation of a Young Offender. K. E. Rose.—p. 838.

Mirth Response Test: A Psychodiagnostic Technique.—On the basis of Freud's theory, humor is an important index to dynamic forces within the individual personality. In psychopathological conditions behavior related to humor is often disturbed. When

the individual has difficulty in expressing humor freely, it may be inferred that other more stressful emotions are even less easily expressed. Different responses to humorous stimuli may be accounted for by the following assumptions: 1. When a stimulus elicits a humorous response, it is assumed that there has been a momentary release of some suppressed or repressed need, without the usual accompanying anxiety. 2. When a stimulus, ostensibly humorous, is responded to with indifference, it is assumed that either (a) no "conflictual" needs are involved, (b) the needs are so deeply repressed that no affective participation is possible, or (c) rigid ego control is involved. 3. When an ostensibly humorous stimulus evokes anxiety, disgust, shame, guilt, or horror, it is assumed that the release of some primary suppressed or repressed need produces a threat with the resulting affect of displeasure. On these assumptions is based a test tentatively named the Mirth Response Test (MRT). In this test a series of 36 popular cartoons are presented to a subject. Three successive procedures involve the observation and recording of different forms of expressive and verbal responses to these humorous stimuli. The three steps are Free Expression, Sorting, and Inquiry. Many of the 83 subjects tested had been studied clinically. Correlation of test results with clinical findings tends to corroborate Freud's theory of humor and the three postulates derived from it. Analysis of the test findings leads to inferences about the subject's aggressive sexual and dependent needs, and the defenses mobilized against their expression. Diagnostic and dynamic formulations were made concerning each subject. These were checked against clinical diagnoses and overt symptoms. Certain aspects of intellectual and emotional functions were also manifest in the test.

American Journal of Psychotherapy, New York

5:495-718 (Oct.) 1951. Partial Index

- Dynamic Role of Group Therapy in Total Treatment Program of Psychotic Patients. W. Goldfarb and P. D. Park.—p. 514.
- Dreams of Finding Money. R. M. Griffith.—p. 521.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

66:701-872 (Nov.) 1951

- The Radiologist as a Physician. H. D. Kerr.—p. 701.
- Electronic Amplification of Roentgenoscopic Image: Present Status of Moon's Scanning Tube Method. P. C. Hodges and L. S. Skaggs.—p. 705.
- Roentgenographic Findings in Congenital Tricuspid Atresia with Hypoplasia of Right Ventricle. M. H. Wittenborg, E. B. D. Neuhauser and W. H. Sprunt.—p. 712.
- Early Roentgen Diagnosis in Acute Bleeding from Upper Gastrointestinal Tract: II. Roentgen Aspects. M. Ritvo, T. P. Cotter and N. Zamcheck.—p. 728.
- Symptomless Pulmonary Arteriovenous Aneurysms or Fistulas. D. J. Roberts and J. E. Hutchison.—p. 743.
- Suprahepatic Interposition of Colon and Volvulus of Cecum. J. Torgersen.—p. 747.
- Importance of Minor Myelographic Deformities in Diagnosis of Posterior Protrusion of Lumbar Intervertebral Disc. G. F. Boulton, M. K. Kiernan and A. E. Child.—p. 752.
- Preliminary Report on Telepaque, New Cholecystographic Medium. W. R. Christensen and M. C. Sosman.—p. 764.
- Ioduron B Bronchography: Preliminary Report of Study with Water-Soluble Contrast Medium. L. C. Brandenstein.—p. 769.
- *Endometriosis: Its Management and End Results. R. A. Hays and U. V. Portmann.—p. 773.
- Malignancy in the Negro: Statistical Review. B. W. Robinson.—p. 783.
- Physical Measurements on Various Beta-Ray Applicators. J. S. Krohmer.—p. 791.
- Secondary Alterations of Frontal Sinus in Cancer of Paranasal Sinuses. L. L. Haas.—p. 797.
- Artefacts Simulating Minimal Pulmonary Tuberculosis. I. J. Kane.—p. 803.
- Videogonosis: Roentgenologic Television Diagnosis. Service for the Small Community Hospital. J. Gershon-Cohen.—p. 808.

Endometriosis: Its Management and End Results.—Hays and Portmann review 142 cases of endometriosis seen at the Cleveland Clinic from 1939 to 1949. Acquired and progressive dysmenorrhea is the commonest symptom of endometriosis, and occurred in 57% of these cases; excessive menses occurred in 41.5%. Other complaints, such as headache, pelvic pain, rectal distress, and dyspareunia, occurred less frequently. Physical findings included painful pelvic masses or small nodules along the uterosacral ligaments. Of the married women, 37.1% were

sterile. The ovary is the commonest site of involvement (58.5%), followed by the uterus, cul-de-sac, uterosacral ligament, and rectovaginal septum. Treatment depends on the age of the patient, extent of involvement, and severity of symptoms. Since ovarian function is necessary for continued growth of ectopic endometrium, ablation of the ovaries by surgery or irradiation results in relief of symptoms and regression of the lesions. Preservation of some ovarian activity by conservative measures is desirable whenever possible. A table classifying the results of various treatments indicates that of the 82 patients subjected to surgical treatment (radical or conservative), 63 obtained good and 9 fair results, and the remaining 10 had poor results. Irradiation therapy was employed in 34 patients, and the results were good in all but one. Results of treatment with hormones were disappointing.

American Surgeon, Atlanta, Ga.

17:993-1090 (Nov.) 1951

- Female Urologic Disorders Which Cause Abdominal Pain. G. J. Thompson.—p. 993.
 Acute Pancreatitis: Report of Two Cases with Review of Literature. W. G. Ellis.—p. 1000.
 Intramedullary Spinal Cord Metastases from Melanomas: Report of Unusual Case and Review of Literature. C. B. Clay and A. H. Weiland.—p. 1009.
 Treatment of Pseudocysts of Pancreas by Internal Drainage. T. C. Moore and H. B. Shumacker Jr.—p. 1018.
 Malignant Tumors of Thyroid. N. S. Shofner.—p. 1025.
 Training Courses for Ambulance Drivers. C. C. Howard.—p. 1036.
 Acute Intestinal Obstruction in Infants and Young Children. M. L. Michel Jr. and M. L. Jarrell.—p. 1040.
 Management of Staghorn Renal Calculi. C. L. Prince, P. L. Scardino and J. C. Presti.—p. 1057.
 Treatment of Fractures with Intramedullary Nail. C. W. Perry.—p. 1064.

Annals of Internal Medicine, Lancaster, Pa.

35:763-960 (Oct.) 1951

- New Problems in Treatment of Infectious Diseases. C. P. Miller.—p. 763.
 Preventive Immunization in National Emergency. R. E. Dyer.—p. 771.
 Air Embolism. A. C. Cohen, G. C. Glinsky, G. E. Martin and K. I. Fetterhoff.—p. 779.
 *Gastric Antacid and Anti-Secretory Drugs: Survey Based Primarily on Their Effects upon Gastric Secretion in Man. J. B. Kirsner, W. L. Palmer, E. Levin and A. P. Klotz.—p. 785.
 Test for More Accurate Recognition of Gall-Bladder and Liver Bile During Diagnostic Biliary Drainage. A. A. Hall and J. M. Masen.—p. 812.
 ectasis of Right Middle Lobe Resulting from Perforation of Tuberculous Lymph Nodes into Bronchi in Adults. A. G. Cohen.—p. 820.
 Hypercholesterolemia: Analysis of 529 Cases and Treatment of 297 by Low Animal Fat Diet and Desiccated Thyroid Substance. W. W. Priddle.—p. 836.
 Rationale of Geriatric Medicine. E. J. Stieglitz.—p. 848.
 Therapy of Traumatic Shock. B. Burbank.—p. 857.
 Myocardial Infarction in Rural Hospital. F. F. Harrison.—p. 872.
 Pain in Acute and Chronic Diseases of Liver. H. P. Lewis.—p. 878.
 Some Social Implications of Medical Progress. F. G. Dickinson.—p. 889.

Gastric Antacid and Anti-Secretory Drugs.—The goal of treatment with antacid and antisecretory drugs presumably is neutralization or inhibition of the free acid and peptic activity of the gastric secretion. None of the available antacids completely neutralizes free acid in man for prolonged periods, but calcium carbonate appears to be the most effective antacid in current use. In hourly doses of 2 or 4 gm., together with milk and cream and atropine in doses of 1.0 gm. two to four times daily, calcium carbonate usually maintains the pH of the gastric contents between 4.0 and 5.5 in patients with duodenal ulcer; it does not cause alkalosis and its constipating effect can be corrected with laxative antacids. This regimen, however, is effective only during the period of administration; it does not control excessive nocturnal gastric secretion. Calcium carbonate administered by continuous intragastric drip is perhaps more effective for this purpose, but its applicability is limited. Aluminum hydroxide, magnesium trisilicate, or tribasic calcium phosphate in large quantities diminish but do not completely eliminate the free acidity; their neutralizing effect is much less or zero when administered at long intervals and in small amounts. The antacid efficiency of sodium carboxymethylcellulose in man remains to be determined. Protein hydrolysates are less effective than calcium carbonate even in large amounts, and they provoke a secondary rise in secretion exceeding original levels. The neutralizing effect of available resins in vivo is not impressive. De-

tergents such as sodium alkyl sulfate do not alter the pH of the gastric contents, and their antipeptic action in man is insignificant. Mucin has little neutralizing value. Antihistaminic agents do not depress gastric secretion in man. With the possible exception of chorionic gonadotropin and the combination of chorionic gonadotropin and estrogen, the inhibitory effect of various sex hormones, injected intramuscularly in large amounts, appears minimal. Other hormones, such as parathyroid extract, desoxycorticosterone acetate, and corticotropin (ACTH) also do not inhibit gastric secretion in vivo. Atropine produces extremely variable effects in patients with duodenal ulcer; its principal usefulness may be to enhance antacid action by prolonging gastric emptying. In contrast to atropine and to synthetic atropine-like compounds, the results thus far obtained with other cholinergic blocking agents are promising. Tetraethylammonium salts significantly depress gastric secretion and motility in man, but there are undesirable side reactions. Hexamethonium compounds have yielded promising preliminary results. Methantheline (banthine®) bromide given parenterally apparently inhibits gastric secretion more effectively with fewer toxic manifestations. Although there is no evidence that these agents induce the physiological effects expected from complete vagotomy, they may permit in many ulcer cases a more liberal regimen of antacids and diet.

Hypercholesterolemia.—Estimations of serum cholesterol were performed on 1,089 patients seen in an internal medicine practice. Cholesterol levels above 250 mg. per 100 cc. were found in 529 (48.6%). Of these 529 patients, 267 (50.5%) had levels over 300 mg. per 100 cc. Of the 1,089 patients, 768 (70.5%) were over 40 years of age, and 450 (59%) of these had an elevated serum cholesterol level. There was a consistent increase in hypercholesterolemia with advancing age. Of 160 patients with arteriosclerosis, 116 (72.5%) had elevated serum cholesterol levels. Of 86 patients with coronary arteriosclerosis 60 (69.7%) had hypercholesterolemia. Approximately the same percentage was established for patients with retinal arteriosclerosis, hypertension, and diabetes mellitus. Treatment was given to 297 patients with hypercholesterolemia: 34 were treated with desiccated thyroid substance, 49 with diet low in animal fat, and 214 with both a low animal fat diet and desiccated thyroid substance, for from six months to three years. Although the average serum cholesterol levels of these patients were lower at the end of the period of treatment than at the beginning, the results were not pronounced or consistent. In 27 (55%) of the 49 patients the serum cholesterol level was lower with the low animal fat diet. With the administration of desiccated thyroid substance, and the combination of low animal fat diet with desiccated thyroid substance, the serum cholesterol level was decreased in approximately 45% of patients in each group. Further studies are in progress.

Annals of Western Medicine & Surgery, Los Angeles

5:815-898 (Oct.) 1951

- *Biochemical Basis of Betaine-Glycocyamine Therapy. H. Borsook and M. E. Borsook.—p. 825.
 *Treatment of Cardiac Decompensation with Betaine and Glycocyamine. M. E. Borsook and H. Borsook.—p. 830.
 New Biochemical Approach to Treatment of Congestive Heart Failure. V. Van Zandt and H. Borsook.—p. 856.
 Use of Betaine and Glycocyamine in Treatment of Patients with Heart Disease: Preliminary Report. A. Graybiel and C. A. Patterson.—p. 863.
 Forensic Medicine: Forensic Science Practice in Smaller Communities. K. M. Dubowski.—p. 876.
 Practical Medicine: Hemorrhage Complicating Pregnancy and Labor. K. P. Russell.—p. 882.

Biochemical Basis of Betaine-Glycocyamine Therapy.—This paper supports the hypothesis that larger than normal amounts of creatine may be beneficial in conditions of muscular weakness or degeneration, including cardiac failure, and in some neurological conditions. The immediate precursor of creatine in the animal is glycocyamine (guanidoacetic acid). It is synthesized from arginine and glycine in the kidney. Glycocyamine is then transported to the liver where it is methylated by methionine to form creatine. But there is experimental evidence that betaine can supply the necessary methyl group. After explaining in more detail the biochemical processes involved in betaine-glycocyamine therapy the Borsooks say that during the last year over 200 patients have taken glycocyamine with betaine. The daily

dose, by mouth, is glycocyamine, 30 mg. per pound of body weight, and betaine hydrate four to five times the dose of glycocyamine. The two substances were taken together, the glycocyamine in tablets, the betaine dissolved in water, and the total daily dose divided into four or five portions through the day. The daily ingestion of betaine and glycocyamine at these levels may be considered nontoxic in view of experimental and clinical data. Analyses of blood and urine revealed nothing that would indicate a toxic effect of betaine or glycocyamine, and no symptoms suggested toxic effects.

Betaine and Glycocyamine in Cardiac Decompensation.—

Betaine and glycocyamine were given over a period of 6 to 10 months to 28 patients with cardiac decompensation. In 20 of these patients, betaine and glycocyamine medication was the only treatment used. These patients remained free of signs and symptoms of cardiac decompensation. In four patients, betaine and glycocyamine were added to other therapy; in three, betaine and glycocyamine therapy failed in that two patients had a coronary occlusion, and one patient had a recurrence of rheumatic fever. An improved sense of well-being, less fatigue, and greater strength and endurance was observed in nearly all patients. These effects persisted but their relation to improved cardiac function was not always evident. Most of the patients gained weight, which was not due to edema and probably was, in part, due to a positive nitrogen balance and the effects of improved rest and better appetite. In 18 patients with hypertension, the blood pressure fell shortly after betaine and glycocyamine therapy was begun. The decrease in blood pressure persisted in four of these. A large increment in the total creatinine excretion (creatinine plus creatinine) was observed in all patients. An endocrine effect was suggested in that one-third of the patients, both men and women, reported increased libido. Some of the women reported enlargement of the breasts. The signs and symptoms of arthritis and asthma decreased. The only untoward effects observed were transient nausea and diarrhea, which cleared up spontaneously. The dextrose tolerance of both diabetic and non-diabetic patients was increased.

Blood, New York

6:963-1212 (Nov.) 1951. Partial Index

- Recent Studies on Etiology and Nature of Leukemia. J. Furth.—p. 964.
- Influence of Age and Sex upon Frequency and Cytologic Types of Human Leukemias. Evidence of Myeloid: Lymphoid Antagonism. J. Dausset and V. Schwarzman.—p. 976.
- *Congenital Leukemia. W. G. Bernhard, I. Gore and R. A. Kilby.—p. 990.
- *Observations on Effect of Various Folic Acid Antagonists on Acute Leukemia. S. J. Wilson.—p. 1002.
- Average Volume of Leukemic Leukocytes. H. Tivey, J. G. Li and E. E. Osgood.—p. 1013.
- Effect of Transfusion Polycythemia upon Bone Marrow Activity and Erythrocyte Survival in Man. F. R. Birkhill, M. A. Maloney and S. M. Levenson.—p. 1021.
- Hematologic Changes with ACTH and Cortisone Therapy of Rheumatoid Arthritis. S. C. Finch, C. L. Crockett Jr., J. F. Ross and T. B. Bayles.—p. 1034.
- Demonstration by Nadi Reaction of Cytochrome Oxidase Activity in Cells of Lymphoid and Myeloid Series Obtained from Normal Individuals and Patients Suffering from Hodgkin's and Other Diseases. G. T. Hoffmann, A. Rottino and K. G. Stern.—p. 1051.
- Hematologic Aspects of Disseminated (Systemic) Lupus Erythematosus. S. R. Michael, I. L. Vural, F. A. Bassen and L. Schaefer.—p. 1059.
- Hereditary Spherocytosis: I. Clinical, Hematologic and Genetic Features in 28 Cases, with Particular Reference to Osmotic and Mechanical Fragility of Incubated Erythrocytes. L. E. Young, M. J. Izzo and R. F. Platzer.—p. 1073.
- Id.: II. Observations on Role of Spleen. L. E. Young, R. F. Platzer, D. M. Ervin and M. J. Izzo.—p. 1099.
- Simplified Technique of Spectrography and Its Application to Study of Intracellular Hemoglobin. W. K. Metcalf.—p. 1114.
- Weakly Reacting Rh Positive (D⁺) Bloods. R. E. Rosenfield, P. Vogel, E. B. Miller and G. Haber.—p. 1123.
- Rhesus Antibody Anti-E in Pregnancy and Blood Transfusion: I. Frequency of Occurrence of Pure Anti-E. Report of 12 Cases. II. Demonstration by Pure Anti-E Serum of Dosage Effect of Antigen E in Presence or Absence of Antigen D. R. H. Malone and I. Dunsford.—p. 1135.
- Effects of Hemoglobin Solutions on Renal Functions in Man. J. L. Brandt, N. R. Frank and H. C. Lichtman.—p. 1152.
- Intravenous Iron: Evaluation of Use of Saccharated Iron Oxide in Iron Deficiency States in Obstetrics and Gynecology. B. G. Holly.—p. 1159.

Congenital Leukemia.—Congenital leukemia is exceedingly uncommon, but 14 cases (in eight boys and five girls and one whose sex was not given) were selected from the literature with acceptable evidence of a leukemic state at birth. Significant

physical manifestations are spontaneous hemorrhages of skin and mucous membrane, nodular skin infiltrations, enlargement of spleen and liver, adenopathy, fever, and pallor. The blood should reflect an alteration of the marrow by showing an undue proportion of poorly differentiated or undifferentiated cells, usually of the granulocytic series; all but two of the cases described in the literature were of the granulocytic variety. In most cases considerable elevation of the white blood cell count and reduced numbers of red cells and platelets were also observed. In only 1 of the 14 cases was recognition of the nature of the characteristic hematological disturbance delayed; in this case a diagnosis of congenital thrombocytopenic purpura was made during life, but could not be substantiated by postmortem observations. The authors report four new cases of congenital leukemia in three boys and one girl. Congenital anomalies in three of these patients indicated a growth disturbance early in fetal life. Contrary to the usual finding in childhood leukemia, cells of the granulocytic series in the authors' four patients had a fair degree of differentiation and in this respect were similar to those that characterize the chronic form of the disease. It seems likely, therefore, that the leukemia existed during a significant portion of uterine life. None of the mothers had leukemia, and since there are many reported cases of normal children born to frankly leukemic women, the presence of a blood dyscrasia in the mother does not appear to be of etiological significance.

Folic Acid Antagonists and Acute Leukemia.—Of 70 patients with acute leukemia treated with various folic acid antagonists, 65 survived long enough for evaluation of the effect of the therapeutic agents. Of the 65 patients, 38 had acute lymphatic leukemia, 23 had acute monocytic leukemia, and 4 had acute myelogenous leukemia. The following folic acid antagonists were administered either intramuscularly or orally: 4-aminopteroylglutamic acid ("aminopterin") with an effective dosage of 0.5 to 1.0 mg. per day, 4-amino-N¹⁰ methyl pteroylglutamic acid ("a-methopterin") with a dosage of 3 to 5 mg. per day, 4-amino pteroylaspatic acid ("amino-an-fol") with a dosage of 20 to 30 mg. per day, and 4-amino-9 methyl pteroylglutamic acid ("a-ninopterin") with a dosage of 1.5 to 1.0 mg. per day. The clinical and hematological response to folic acid antagonists was most favorable in acute lymphatic leukemia. Of the 65 patients observed, an excellent clinical and hematological remission occurred in 11 patients, a partial remission in 19, and no response in 35. Although the most satisfactory results were observed in patients between the ages of 3 and 10, excellent remissions were produced in patients between the ages of 42 and 56. When a response occurred, a rather definite hematological pattern was noted. An increased platelet count in most instances was the first evidence of regeneration and occurred in about the third or fourth week. The neutrophilic polymorphonuclear leukocytes began to regenerate at about the same time and an increase in their number was followed by a rise in the erythrocyte count. Observations of the bone marrow indicated that although excellent clinical and hematological remissions might occur, primitive leukemic cells were still present. In some instances megaloblasts were observed in addition to a peripheral macrocytosis and anisocytosis of erythrocytes. Toxic manifestations were common. These included glossitis, ulceration of the oral cavity, nausea, vomiting, diarrhea, and alopecia. In one instance there was ulceration of the entire gastrointestinal tract, including the esophagus and colon. Hematological toxic reactions included thrombocytopenia, leukopenia, and anemia. Aplasia of bone marrow was observed in one instance. In many instances the margin of safety between a toxic reaction and death was small. It should be emphasized that no patient with leukemia has been cured with folic acid antagonists although prolonged remissions have been obtained.

GP (J. Am. Acad. Gen. Practice), Kansas City, Mo.

4:1-216 (Nov.) 1951

- How the Endoscopist Can Help. E. B. Benedict.—p. 34.
- Use of Anticonvulsant Drugs. S. Carter.—p. 41.
- Psychologic Aspects of Plastic Surgery. C. L. Straith and D. R. Millard Jr.—p. 47.
- Breast Feeding of Normal Infants. E. H. Watson.—p. 53.
- Evaluating Psychosomatic Disorders. I. Stevenson.—p. 59.
- Which Anti-Infective to Use? W. C. Cutting.—p. 65.
- Treatment of Liver Disease. R. B. Capps.—p. 69.

Journal Clin. Endocrinology, Springfield, Ill.

11:1215-1410 (Nov.) 1951

- p*-Hydroxypropiophenone (PHP) and Other So-Called Pituitary Inhibitors. C. A. Schaffenburg, G. M. Masson, E. P. McCullagh and P. Haour.—p. 1215.
- Further Observations on Urinary Excretion of Water-Soluble Corticosteroids by Normal and Abnormal Subjects. N. B. Talbot, M. S. Wood, J. Worcester and others.—p. 1224.
- Thyroid-Thyrotropic Hormone Balance in Blood of Normal and Endocrinopathic Individuals. S. A. D'Angelo, K. E. Paschkis, A. S. Gordon and A. Cantarow.—p. 1237.
- Protein-Bound Iodine in Serum of Rats Receiving Iodide or Iodine With or Without Goitrogen. T. S. Danowski, S. J. Huff, P. M. Wirth and others.—p. 1254.
- On Mechanism of Iodide Accumulation by Thyroid Gland. J. B. Wyngaarden, J. B. Stanbury and C. H. DuToit.—p. 1259.
- *Use of Thiouracil in Treatment of Metastatic Carcinoma of Thyroid with Radioiodine. J. E. Rall, W. N. Miller, C. G. Foster and others.—p. 1273.
- Malignant Thyroid Tumors Occurring in Mouse After Prolonged Hormonal Imbalance During Ingestion of Thiouracil. H. P. Morris, A. J. Dalton and C. D. Green.—p. 1281.
- Responses to Radioactive Iodine Therapy in Hyperthyroidism, with Special Reference to Cardiac Problems. F. Maloof and E. M. Chapman.—p. 1296.
- *Study and Treatment of 119 Cases of Carcinoma of Thyroid with Radioactive Iodine. B. M. Dobyns and F. Maloof.—p. 1323.
- Foods and Genesis of Goiter. M. B. Fertman and G. M. Curtis.—p. 1361.
- Excretion of Steroidal Substances by Adrenal Cortex in Various Diseases. K. Shadaksharappa, N. O. Calloway, R. H. Kyle and R. W. Keeton.—p. 1383.
- Adrenogenital Syndrome with Associated Episodes of Hypoglycemia. F. P. White and L. E. Sutton.—p. 1395.

Thiouracil in Radioiodine Treatment of Thyroid Metastases.—Iodine concentration by thyroid cancers can be effectively increased by prolonged pretreatment with thiouracil, according to studies made at Sloan-Kettering Institute and Memorial Center. Following total thyroidectomy (either surgical or with radioiodine), thiouracil was administered in doses of from 1.0 to 1.5 gm. per day. Three patterns of response were noted: (1) complete failure of thiouracil to influence radioiodine uptake; (2) gradual increase in avidity of metastatic lesions for radioiodine; and (3) abrupt development of extremely high uptake. Increased uptake resulting from preparation with thiouracil made it possible to administer therapeutic doses of radioiodine to 16 patients. Pulmonary metastases diminished in three cases; growth was arrested in skeletal metastases in three others; and some improvement was noted in all. Six patients obtained relief from pain. Toxic effects resulting from the use of thiouracil were slight. There was no agranulocytosis, although in many patients a leukopenia of 3,000 cells per cubic millimeter developed. Discontinuance of thiouracil was necessary in one case because the patient had a severe urticaria.

Radioactive Iodine in Thyroid Carcinoma.—Radioactive iodine was used to study, and in some instances to treat, 119 patients with carcinoma of the thyroid. The initial uptake of the isotope in these carcinomas and their metastases is less than that of normal thyroid. As a result the quantity collected is so small that it has little if any therapeutic value. Three methods of increasing the uptake are described: total thyroidectomy, destruction of normal thyroid function with radioactive iodine, and use of thiouracil compounds. A demonstrable increase in the uptake of radioactive iodine in metastases has been shown to follow total thyroidectomy; the interval between the operation and the appearance of the increase varies from three or four days to six months. Uptake usually becomes more pronounced as time passes. Use of radioactive iodine to destroy normal thyroid function has several disadvantages: the amount required is relatively large and adds to the total radiation received by the patient; the first dose may be inadequate, necessitating further doses; and, valuable time is lost. The possibility that the malignancy can be removed by surgery, or that the lesion is encroaching upon the trachea or esophagus, makes surgical exploration, and possibly operation, advisable in most cases. Thiouracil compounds block the uptake of radioactive iodine in metastases, causing eventual depletion of stored iodine. Subsequent withdrawal of thiouracil finds the tumor avid for iodine and increases uptake. Use of radioactive iodine in therapeutic doses ranging from 50 to 200 mc. benefited 10 of 50 patients with known metastatic lesions remaining after total thyroidectomy. Radiation from

radioactive iodine commonly causes a decline in the circulating lymphocytes. No other serious blood changes were observed in this series. Ovarian failure and inflammatory reaction in the urinary bladder occurred in patients with pelvic metastases, apparently as a result of proximity, and liver damage was noted in one patient.

Journal Lab. and Clinical Medicine, St. Louis

38:663-828 (Nov.) 1951. Partial Index

- Localization of Radioactive *L*-Thyroxine in Neurohypophysis. J. M. Jensen and D. E. Clark.—p. 663.
- Diabetogenic Action of Organic Reagents: Destructive Lesions of Islets of Langerhans Caused by Sodium Diethyldithiocarbamate and Potassium Ethylxanthate. I. Kadota and O. Midorikawa.—p. 671.
- Impairment of Liver Function Subsequent to Injury to Spinal Cord. I. S. Cooper, E. H. Rynearson and C. S. MacCarty.—p. 689.
- Importance of Serial Determinations of Serum Alkaline Phosphatase in Incomplete Biliary Tract Observation. H. Ulevitch, E. A. Gall, P. I. Hoxworth and others.—p. 693.
- Effect of Single Large Doses of Choline or Methionine on Phospholipid Turnover in Normal Human Subjects Maintained on Low-Protein Diet for Seven Days. W. E. Cornatzer, D. Cayer and W. A. Lambeth Jr.—p. 705.
- Rutin—Its Effect on Eosinophil Count in Peripheral Blood of Normal Subjects. J. Dougherty and J. K. Meneely Jr.—p. 709.
- Studies on Relationship of Tissue Fluid and Blood Levels of Penicillin. L. Weinstein, G. K. Daikos and T. S. Perrin.—p. 712.
- Cross-Resistance to Antibiotics: Effect of Repeated Exposure of Bacteria to Aureomycin, Terramycin, Chloramphenicol or Neomycin on Resistance to All of These Antibiotics and to Streptomycin and Penicillin. T. M. Gocke and M. Finland.—p. 719.
- Middlebrook Hemagglutination Test for Tuberculosis: Evaluation in Normal Subjects and in Patients with Tuberculosis. J. Adcock, R. R. Haley and W. N. Davey.—p. 736.
- Fatal Herpes Simplex Infection in Newborn Infant. J. J. Quilligan Jr. and J. L. Wilson.—p. 742.
- Simultaneous Recovery of Type A' and Type C Influenza Viruses from Patient. E. Minuse and F. M. Davenport.—p. 747.
- Simplified Titrimetric Techniques for Assay of Calcium and Magnesium in Plasma. E. S. Buckley Jr., J. G. Gibson II, and T. R. Bortolotti.—p. 751.
- Specificity of Desiccation Method for Determining Alcohol in Biological Fluids. H. W. Smith.—p. 762.

Journal of Nutrition, Philadelphia

45:165-304 (Oct.) 1951. Partial Index

- Excretion of Two Biologically Active Forms of Ascorbic Acid and of Diketogulonic Acid by Human Subjects. S. D. Chen and C. Schuck.—p. 165.
- Nitrogen Balance of Adult Rats Fed Diets Low in L- and DL-Threonine. E. S. Nasset, J. T. Anderson and A. M. Siliciano.—p. 173.
- Calories—Limiting Factor in Growth of Children. I. G. Macy and H. A. Hunscher.—p. 189.
- Calcium Balance of Adult Human Subjects on High- and Low-Fat (Butter) Diets. F. R. Steggerda and H. H. Mitchell.—p. 201.
- Study of Test Dose Excretion of Five B Complex Vitamins in Man. F. T. Lossy, G. A. Goldsmith and H. P. Sarett.—p. 213.
- Leucine and Histidine Tolerance in the Human. B. F. Steele and C. B. Le Bovit.—p. 235.
- Study of Histidine Deficiency and Nitrogen Balance Under Ad Libitum and Force-Feeding Conditions. J. W. Bothwell and J. N. Williams Jr.—p. 245.
- Reproductive Failure of Rats on Glyceryl Trilaurate-Containing Diets and Its Prevention by Certain Natural Fats. K. W. Keane, E. M. Cohn and B. C. Johnson.—p. 275.

J. Pharmacology & Exper. Therap., Baltimore

103:107-214 (Oct.) 1951. Partial Index

- Effect of Certain Antihistaminics on Epinephrine-Induced Hyperglycemia and Lacticacidemia. E. L. Komrad and E. R. Loew.—p. 115.
- Metabolic Action of Cardiac Glycosides: II. Effect of Ouabain and Digoxin on Energy-Rich Phosphate Content of Heart. A. Wollenberger.—p. 123.
- Mode of Action of Sodium Diphenylhydantoinate (Dilantin) in Epilepsy. R. B. Aird and L. Strait.—p. 136.
- Elimination of Enzymatic Diffusion Artifacts in Histochemical Localization of Cholinesterases and Survey of Their Cellular Distributions. G. B. Koelle.—p. 153.
- Effect of dl-Amphetamine Sulfate and Its Isomers on Intestinal Motility. E. J. Van Liere, J. C. Stickney, D. W. Northup and R. O. Bell.—p. 187.
- Effect of Intravenous Administration of Pitressin on Renal Function in Man. M. H. Maxwell and E. S. Breed.—p. 190.
- Relationship of Human Plasma Proteins in Action and Transport of Penicillin. B. Halpern, R. E. Dolkrat, J. B. Lesh and others.—p. 202.
- Excretion and Tissue Distribution Studies on Radioactive Nicotine. A. Ganz, F. E. Kelsey and E. M. K. Geiling.—p. 209.

Mental Hygiene, Albany, N. Y.

35:529-712 (Oct.) 1951. Partial Index

- Community Psychiatry and Its Organizational Problems. G. Frankl.—p. 532.
 Principles and Practices Used in Child Psychiatric Clinics. H. W. Newell—p. 571.
 Psychodynamics of the Triad, Alcoholism, Gambling, and Superstition. I. Galdston.—p. 589.
 Volunteer Work in State Hospital by College Students. J. N. Haddock and H. D. Dundon.—p. 599.
 Organizing for Mental Health in the Local Community. S. Whitman.—p. 618.

Ohio State Medical Journal, Columbus

47:981-1084 (Nov.) 1951

- Polyarteritis Nodosa: Review Together with Report of Case Due to Hydantoin Sensitization Treated with Cortisone. A. L. Frankel and N. O. Rothermich.—p. 1013.
 The National Diabetes Detection Drive—November 11-17, 1951. T. P. Sharkey.—p. 1022.
 Erythema Infectiosum: Fifth Disease—Clinical Note. R. I. Fried.—p. 1027.
 Cancer of Cervix—The General Practitioner's Enigma. L. B. Greentree.—p. 1029.
 Evaluation of Antithyroid Drugs in Management of Goiter. R. C. Austin and E. F. Damstra.—p. 1032.

Oklahoma State Medical Assn. J., Oklahoma City

44:419-458 (Nov.) 1951

- Hyperparathyroidism-Osteitis Fibrosa Cystica Parathyroid Adenoma with Report of Case. J. C. Brogden and L. Lowbeer.—p. 421.
 Studies of Treatment Problems of Adenocarcinoma of Endometrium. J. L. McKelvey.—p. 428.
 The Newer Antibiotics. R. Q. Goodwin.—p. 432.
 Care of the Burned Patient. A. R. Wiley.—p. 436.

Public Health Reports, Washington, D. C.

66:1379-1414 (Oct. 26) 1951

- Dental Practice in Western Pennsylvania. A. Ciocco, I. Altman and I. Sissman.—p. 1379.
 Domestic Water and Dental Caries: VII. Study of Fluoride-Dental Caries Relationship in Adult Population. A. L. Russell and E. Elvove.—p. 1389.
 *Viability of *Brucella Melitensis* in Naturally Infected Cured Hams. L. M. Hutchings, N. B. McCullough, C. R. Donham and others.—p. 1402.

66:1415-1450 (Nov. 2) 1951

- Field Studies on Immunization Against Tuberculosis: I. Tuberculin Allergy Following BCG Vaccination of School Children in Muscogee County, Georgia. L. W. Shaw.—p. 1415.
 Research Contributions of BCG Vaccination Programs: II. Tuberculin Sensitivity at Different Altitudes of Residence. L. E. Bates, T. Busk and C. E. Palmer.—p. 1427.

Viability of *Brucella* in Naturally Infected Cured Hams.—Eleven yearling hogs weighing from 300 to 400 lb. (136.2 to 181.6 kg.) were obtained from a herd exhibiting clinical evidence of brucellosis. Numerous abortions prompted the owner to dispose of the herd. The hogs all had positive *Brucella* agglutination tests. All cultures obtained from these hogs were identified as *Br. melitensis*. Prior to slaughter, blood for culture was obtained from each animal. The hogs were slaughtered and processed in an improvised abattoir closely simulating packing plant conditions. Cultures made from many areas of the carcass showed the organism to be widely distributed. The hams and shoulders were cured by standard processes, 11 hams subsequently being smoked. *Brucella* was recovered from the hams for as long as 21 days in cover pickle, but the organism was not recovered after the smoking process. These data should not be interpreted to mean that all commercial smoking processes make *Brucella* nonviable, or that home-smoked meats are necessarily safe.

Rocky Mountain Medical Journal, Denver

48:811-908 (Nov.) 1951

- Geriatric Abdominal Surgery. R. M. duRoy and K. C. Sawyer.—p. 834.
 Preventing Socialized Medicine Is Our Job: Presidential Address. K. E. Krueger.—p. 842.
 Indications and Contraindications for Cesarean Section. E. S. Auer.—p. 844.

South Carolina Medical Assn. Journal, Florence

47:393-434 (Nov.) 1951

- Scopolamine in Obstetrics. H. F. Sharpley Jr.—p. 393.
 Drug Therapy in Allergic Disease. I. M. Hinnant.—p. 401.
 Sympathectomy for Hypertension Follow-Up Survey. F. E. Kredel, G. S. T. Peebles and B. Wham.—p. 406.

Surgery, St. Louis

30:763-922 (Nov.) 1951

- Surgical Treatment of Massive Lymphedema of Lower Extremities. D. A. Campbell, W. W. Glas and M. M. Musselman.—p. 763.
 Chronic Portal Vein Occlusion and Portal Hypertension in Dog. A. N. Morris and H. H. Miller.—p. 768.
 Observations on Complete Reversal of Circulation in Hind Limb of Dog. T. B. Ferguson, W. C. Sealy, W. G. Young and R. A. Gowdy.—p. 775.
 Simple Electrical Apparatus for Clinical Treatment of Ventricular Fibrillation. W. B. Kouwenhoven and J. H. Kay.—p. 781.
 *Anterior Chamber of Eye for Investigative Purposes: Site for Transplantation of Fetal Endocrine Tissues and Cancer, and for Study of Tissue Reaction. J. T. Dameron.—p. 787.
 Clinical Physiology of Human Bronchi: II. Effect of Vagus Section upon Pain of Tracheobronchial Origin. D. R. Morton, K. P. Klassen and G. M. Curtis.—p. 800.
 Bronchial Arteries: I. Experimental Occlusion. F. H. Ellis Jr., J. H. Grindlay and J. E. Edwards.—p. 810.
 Incidence of Distant Metastases Among Patients Dying with Head and Neck Cancers: Analysis of 200 Autopsies. L. F. Peltier, L. B. Thomas, T. H. Crawford and others.—p. 827.
 Experimental Use of Free Arterial and Split-Thickness Skin Grafts for Bridging Defects in Common Bile Duct of Dog. C. A. Hardin and C. F. Kittle.—p. 834.
 Primary End-to-End Anastomosis for Congenital Atresia of Small Bowel. I. D. Baronofsky.—p. 841.
 Effect of Hyaluronidase and Plasma Administered Subcutaneously to Burned Rats. K. L. Stephenson.—p. 845.

Transplantations into Anterior Chamber of Eye.—The anterior chamber of the eye is adapted for the study of problems that are not necessarily ophthalmologic. It was used by the author in the study of tissue reaction to foreign materials, the homologous transplantation of fetal endocrine tissue in adult nonrelated hosts, and the heterologous transplantation of human cancer. (1) A small piece of polyethylene tubing was inserted into the anterior chamber of a rabbit's eye for over three months. Minimal tissue reaction was observed. It was considered safe, therefore, to place such tubing within the spinal epidural space in order to give analgesia over a period of several weeks to a patient with an inoperable and painful carcinoma. This simple method of studying tissue reaction to foreign bodies does not require histological techniques. By using this method the reaction of the tissues to the foreign bodies may be observed continuously. (2) Fetal transplants were made of adrenal, ovary, testes, and thyroid tissue in 230 rabbits, 170 guinea pigs, and 53 dogs. The hosts were adult unrelated animals. The eye of the host was anesthetized with either 7% cocaine or 1% tetracaine hydrochloride and the endocrine tissue fragments were inserted into the anterior chamber of the eye with the aid of a trocar and guided farther down into the junction of the iris and cornea by external pressure on the cornea. A 50 to 60% survival with continuous growth was obtained in the homologous embryonic transplants of adrenal, ovary, testes, and thyroid tissue in adult normal guinea pigs and rabbits. In castrated and thyroidectomized hosts, the percentage of "takes" of the ovaries and testes and thyroid was increased from 60 to 90%. Results indicated that fetal endocrine transplants of adrenal ovary, testes, and thyroid tissue grow, differentiate from fetal to adult form, and function within the host. In the dog the anterior chamber is very large; because of this, many of the transplants were allowed to flow to the center of the cornea where they died because of lack of blood supply and the percentage of "takes" was less in the dog. (3) A piece of thyroid carcinoma was obtained from a patient at the time of a lymph node dissection of the neck and was transplanted to the anterior chamber of the eyes of a guinea pig. There the cancer grew and was microscopically identical to that obtained from the patient. A malignant melanoma was obtained at the time of operation from a patient and was transplanted within two hours to the anterior chamber of a rabbit's eye. The tumor grew and was microscopically identical to the original tumor. The susceptibility of human malignant tissue to drugs, hormones, or irradiation therapy may advantageously be studied in such a manner.

FOREIGN

Acta Tuberculosea Belgica, Brussels

42:415-486 (Oct.) 1951. Partial Index

- *Some Recent Techniques of Bacteriologic and Serum Diagnosis in Phthisiology. R. Linz.—p. 415.
Abuses of Streptomycin, Paraaminosalicylic Acid and Amithiozone. A. Verstraeten.—p. 455.
Bronchographic Studies During Coughing. R. Péromet.—p. 462.

Diagnosis in Phthisiology.—Smears of 181 sputum specimens of patients with tuberculosis were stained according to the Ziehl-Neelsen method using either methylene blue or strong iodine (Lugol's) solution as counterstains. Tubercle bacilli were demonstrated in 79 of the 181 specimens. In no instance were the tubercle bacilli demonstrated by one of the two counterstains and not by the other, but they were demonstrated more easily and rapidly with the strong iodine solution. For the detection of tubercle bacilli in sputum, gastric washings, cerebrospinal fluid, and urine, culture proved superior to direct microscopic examination but not to guinea pig inoculation. Of 76 positive specimens, 48 (63.2%) were positive on both culture and guinea pig inoculation, 9 (11.8%) were positive on culture and negative on guinea pig inoculation, while 19 (25%) were negative on culture and positive on guinea pig inoculation. Culture of tubercle bacilli carried out concurrently with animal inoculation is advocated. The Middlebrook and Dubos hemagglutination test still requires additional study, and its diagnostic and prognostic significance is not well known. The measurement of in vitro streptomycin-sensitivity of tubercle bacilli detected in the sputum is easy, but interpretation of results obtained in practice is difficult. Streptomycin sensitivity tests are time-consuming, and results may be so delayed that the patient cannot be benefited. Determination of the number of bacilli in the patient, which in turn determines the bacteriostatic concentration of streptomycin, presents other difficulties. Sensitive tubercle bacilli may persist in the patient treated with streptomycin, and occasionally bacilli that became resistant during streptomycin therapy may become sensitive again later. To be clinically significant, the streptomycin sensitivity test requires that the total amount of sputum produced in two or three successive days be studied. Results of sensitivity tests of the same specimen may be contradictory when performed according to different methods. These difficulties necessitate close collaboration between the clinician and bacteriologist.

Archives of Disease in Childhood, London

26:365-476 (Oct.) 1951. Partial Index

- Neurosurgical Methods in Treatment of Tuberculous Meningitis: With Note on Some Unusual Manifestations of Disease. H. Cairns.—p. 373.
Cerebral Palsy. W. R. F. Collis and M. O'Donnell.—p. 387.
Mortality in Young Children in the City of Aberdeen During 50 Years 1900-1949. J. Craig.—p. 399.
*Assessment of Prematurity by Birth Weight, Crown-Rump Length, and Head Circumference. R. W. B. Ellis.—p. 411.
Foetal Adrenal Hyperplasia. C. F. Harris and E. F. Scowen.—p. 423.
Radial Nerve Palsy Associated with Localized Subcutaneous Fat Necrosis in the Newborn. R. Lightwood.—p. 436.
Recurrent Neutropenia. A. Moncrieff.—p. 438.
Convulsions (Including Epilepsy) in Childhood. D. Paterson.—p. 441.
Studies in Coeliac Disease: Glucose Absorption. W. Sheldon and A. MacMahon.—p. 446.
Random Reflections on Human Milk Bank. J. G. Wilson.—p. 452.
Myasthenia Gravis in Children. W. G. Wyllie, M. Bodian and N. F. E. Burrows.—p. 457.

Assessment of Prematurity.—The occipitofrontal head circumference, crown-rump length, and birth weight were measured on 119 living premature infants of 29 to 37 weeks' gestation, and on 243 male and 209 female full term infants. Crown-heel length was measured on 30 premature infants, and on 238 male and 206 female full term infants. The means and standard deviations for groups of increasing gestational age are presented. It is suggested that crown-rump length might usefully be included in the routine measurement of infants where facilities are available, and it is emphasized that this measurement has certain advantages over that of crown-heel length in the case of premature infants. The criteria of prematurity are discussed, and the following arbitrary measurements agreed with the data well enough to be of clinical value: head circumference less than 33 cm. (13 in.); crown-rump

length less than 32 cm. (12½ in.) or alternately less than 12½ in.; birth weight 2,500 gm. (5½ lb.) or less. It is emphasized that any single arbitrary standard is likely to include some full term infants and exclude some premature infants of over 36 weeks' gestation. The proportion of misfits will be reduced by using three or more measurements in combination, together with gestational age when this is known. The correlations of birth weight and crown-rump length to gestational age in weeks in premature infants were almost identical, viz., 0.61 and 0.60, respectively. In full term infants, the crown-heel and crown-rump length showed the highest correlation with weight. The correlations were smallest in the case of head circumference.

Biochemical Journal, London

49:561-720 (Oct.) 1951. Partial Index

- Influence of High-Sucrose Diet on Calcium and Phosphorus Percentage Rat Femur, and Comparison with Its Effect on Enamel and Dentine Rat Incisor Teeth. R. L. Hartles.—p. 574.
Dimensions of Particle of Hyaluronic Acid Complex in Synovial Fluid. A. G. Ogston and J. E. Stanier.—p. 585.
Turnover Number of Cholinesterase. W. K. Berry.—p. 615.
Occurrence of Ascorbic Acid in Walnut (*Juglans Regia*). C. Dagli.—p. 639.
Paper Chromatography of Amines. J. M. Bremner and R. H. Kent.—p. 651.
Beta-(3:4-Dihydroxyphenyl) Ethylamine (Hydroxytyramine) in Normal Human Urine. U. S. von Euler, U. Hamberg and S. Hellner.—p. 66.
Cytochrome System of Adrenal Medulla. C. L. Tsou.—p. 658.
Oxidation in Liver of *L*-Tyrosine to Acetoacetate Through *p*-Hydroxyphenyl-pyruvate and Homogentisic Acid. W. E. Knox and M. LeM. Knox.—p. 686.
Biological Action of Substances Related to Thyroxine: 2. Further Investigations of 3:5-Diiodo-4-Hydroxybenzoic Acid. J. H. Wilkinson, M. Sheahan and N. F. MacLagan.—p. 710.

British Journal of Experimental Pathology, London

32:285-386 (Aug.) 1951. Partial Index

- Observations on Course of Infection with Certain Natural Bacterial Pathogens of Rat in Rats on Protein-Deficient Diets. J. A. R. Miles.—p. 285.
Studies on Staphylococcus Mutation: Naturally Occurring "G" Gonococcal Variant and Its Carbon Dioxide Requirements. J. H. Hale.—p. 307.
Action of Proteolytic Enzymes on Antitoxins and Proteins in Immune Sera: III. Further Studies on Enzyme Systems Which Split Antitoxin Molecule. C. G. Pope and M. F. Stevens.—p. 314.
Use of *V. Cholerae* Filtrates in Destruction of Non-Specific Inhibitors. Ferret Sera. A. Isaacs and A. Bozzo.—p. 325.
Complement-Fixing Antigen of Bact. *Coli* Bacteriophage T5: Its Behaviour During Virus Growth. P. M. Rountree.—p. 341.
Effect on Experimental Tuberculosis of Intravenous Injection of Micrococci. N. P. Markham, A. Q. Wells, N. G. Heatley and H. W. Florey.—p. 353.
Some Histological Aspects of Formalin "Arthritis" in Rats. G. H. Boulton.—p. 377.

British Journal of Plastic Surgery, Edinburgh

4:157-230 (Oct.) 1951

- Possibility of Establishing Skin Banks. H. P. Pickerill.—p. 157.
The "Blue Flap": Method of Treatment. W. Hynes.—p. 166.
Malignant Disease: Some Problems of Diagnosis and Initial Treatment. D. C. Bodenham.—p. 173.
*New Method of Nasal Tip Reconstruction Utilising Local Caterpillar Flap. T. D. Cronin.—p. 180.
Transposed Flaps in Cleft Palate Repair. J. Cuthbert.—p. 185.
Case Report: Treatment of Unusual Case of X-Ray Necrosis. E. F. Hynes.—p. 188.
Treatment of Prominent Ears. P. H. Jayes and R. H. Dale.—p. 193.
New Method of Shaping Deformed Ears. A. Ragnell.—p. 202.
Easy Method to Correct Prominent Ears. M. Gonzalez-Ulloa.—p. 20.
Large Osteoma of Frontal Sinus: Method of Removal to Minimize Sinus Ring and Prevent Deformity. T. Gibson and F. M. Walker.—p. 21.
Treatment of Dupuytren Contracture. M. H. Shaw.—p. 218.
Burns: Some Experiences in Local Care. A. B. Wallace.—p. 224.

New Method of Nasal Tip Reconstruction.—Loss of the tip of the nose, even though of small degree, may nevertheless be of major importance in reconstruction. When replacement with tissue from distant sources, such as forehead, neck or arm, is attempted, differences in texture and color of skin must be considered. It is almost axiomatic in plastic surgery that the use of local tissue is the procedure of choice. The two-stage method here described makes use of local tissue. It utilizes two procedures that are well established in plastic surgery, the V-plasty advancement and the "caterpillar" or "creeping" flap. The cat-

pillar flap is raised with its base or pedicle in the direction in which the flap is to be moved. The distal end is then slid towards the base, developing a fold in the flap at right angles to the surface. After two or more weeks, when the distal end of the flap has become well implanted, the original base or pedicle of the flap is cut loose and the end advanced by using the fold in the flap. Two cases illustrating the use of this method are described.

British Journal of Venereal Diseases, London

27:117-172 (Sept.) 1951. Partial Index

- Veneral Diseases in the British Colonies. A. M. W. Rae.—p. 118.
Some Observations on Gonorrhoea Among West African Negroes. G. H. V. Clarke.—p. 130.
Penicillin in Treatment of Neurosyphilis. W. D. Nicol and M. Whelen.—p. 132.
Keratomia Blennorrhagica: Report of Case and Suggestion Concerning Its Nature. G. Auckland.—p. 143.
Jaundice Following Acetarsol Pessaries. H. D. Crosswell.—p. 150.
Venereophobia in the Male. H. L. Rogerson.—p. 158.

British Medical Journal, London

2:1103-1166 (Nov. 10) 1951

- Impact of Protozoa on World Economic Problems. H. E. Short.—p. 1103.
Radiation Cancer of Pharynx. A. W. G. Goolden.—p. 1110.
Ferrous Sulphate Poisoning in Children. I. O. B. Spencer.—p. 1112.
Childhood Factors in Duodenal Ulcer. T. D. Kellock.—p. 1117.
Unusual Case of Traumatic Heart Disease with Clinical Recovery. R. J. Vakil and M. Lenczner.—p. 1120.
Diathermy Treatment of Angiomata. D. Aiken.—p. 1123.
Use and Interpretation of Fantus Estimation of Urinary Chloride. W. H. Taylor.—p. 1125.
Concentration of Oxygen Reached in Oxygen Tents. C. R. S. Jackson.—p. 1129.

Radiation Cancer of Pharynx.—There have been many examples of radiation cancer of the skin, but only a few cases have been reported in which a tumor developed in the deep tissues as a sequel to external therapeutic irradiation. Goolden describes four patients who developed malignant lesions from 26 to 30 years after they had received irradiation therapy. Three of the patients had received x-ray therapy for thyrotoxicosis and the fourth had been treated with x-rays for tuberculous lymph nodes. The growths that appeared many years later were squamous-celled carcinomas in three cases and a fibrosarcoma in the other. In the three patients treated for thyrotoxicosis the tumors had arisen approximately 4 cm. deep in the center of the irradiated area; all three patients had had severe radiation damage to the skin, two of them requiring excision and plastic repair for either epitheliomatous change or necrosis. The fourth patient had not shown convincing evidence of skin damage, and for this reason it might be doubted that the tumor resulted from irradiation. However, the tumor was in an uncommon site for cancer, and it is hard to believe that its appearance was entirely coincidental.

Canadian Medical Association Journal, Montreal

65:409-522 (Nov.) 1951

- Some Observations on Surgical Treatment of Mitral Stenosis. P. David and E. Gagnon.—p. 409.
Upper Gastro-Intestinal Haemorrhage. D. Macdonald and O. Z. Young.—p. 412.
Morbidity Statistics in Department of Veterans' Affairs. G. A. Winfield.—p. 417.
Fits and Faints. C. Symonds.—p. 422.
Abdominal Aortic Aneurysm. H. Gold.—p. 427.
Lister Epoch in Medicine. D. C. Balfour.—p. 431.
Staphylococcal Pneumonia and Pyoderma in Infancy. A. J. De Pape and D. S. McEwen.—p. 439.
Keloid. J. S. Polson, C. J. Pattee and F. M. Woolhouse.—p. 447.
Adrenal Cortical Insufficiency: Psychological and Neurological Observations. R. A. Cleghorn.—p. 449.
Rupture of Oesophagus. G. F. Strong, R. Wilson and H. E. Taylor.—p. 455.
Electroencephalographic Studies in Diabetes Mellitus. D. R. Wilson.—p. 462.
Nephrocalcinosis. H. Ostry.—p. 465.
Sternal Marrow Aspiration in Miliary Tuberculosis. A. R. Armstrong, W. Anderson and J. H. Lee.—p. 468.

Surgical Treatment of Mitral Stenosis.—In 11 patients with suspected mitral stenosis who submitted to exploration of the mitral valve, commissurotomy was performed in 10. Commissurotomy was not performed in one because palpation of the posterior

leaflet suggested the absence of stenosis. Excellent results were obtained in six patients followed for 3 weeks to 14 months, and good results were obtained in two followed for 1 and 4 months, respectively. Two patients died, one because of a cut by technical error in the anterior leaflet that caused blood to regurgitate at systole, and the other because of cardiovascular collapse. Evaluation of results should be based on subjective observations rather than on auscultation and on changes in the quality and intensity of murmurs. Commissurotomy is indicated particularly in patients with a history of pulmonary edema, hemoptysis, peripheral embolism, and decompensation of the right side of the heart. It should not be performed as a prophylactic measure in patients with well-compensated stenosis. With regard to the operative technique three points are stressed: (1) the posterolateral incision is to be preferred to the anterior incision; (2) "digital fracture," i. e., forcing the finger through, should be done only if it has been preceded by an incision; (3) section of the median commissure, which is harder to identify by palpation than the anterolateral band, should not be attempted.

Chirurg, Heidelberg

22:433-480 (Oct.) 1951. Partial Index

- Efficacy of Various Methods of Osteosynthesis in New, Closed Fractures. C. Häbler.—p. 433.
Simplified Technique of Nailing of Neck of Femur. F. Rehbein and H. Gelbke.—p. 439.
Petrochanteric Fractures and Round Nailing. G. Meins.—p. 443.
Therapeutic Results of Nailed Petrochanteric Fractures (Two-Branched Nail). J. Weis.—p. 445.
Tetanus from Wound Infection. K. Poppe.—p. 451.

Methods of Fixation in New, Closed Fractures.—Although mechanical fixation of the ends of a fractured bone is recognized as valuable in incorrectly healed fractures and pseudarthroses, opinions still differ about its value in new fractures. Häbler shows that Küntscher's closed medullary nailing technic is to be preferred to all other radical or conservative methods, when it produces a stable fixation of the fragments. When the fixation is only "relatively stable," the indications for the Küntscher method should be made more strict. In these cases, conservative methods and "open" methods should be compared with Küntscher's method. Binding the fragments together with ring or wire has proved valuable in long oblique fractures of centrally constricted bones and is superior to conservative therapy, but this method is not suitable for short oblique and transverse fractures. The use of wire suture or a spring in the cancellous bone [Maatz] is valuable in fractures in which axial separation threatens (olecranon and patella). The screw method has advantages in the short oblique and Y-fractures at the articular terminations of the long tubular bones, where it is superior to medullary nailing, but it should be resorted to only if nonsurgical reduction does not succeed. Lane's plate, even today, has its place in the treatment of transverse epiphyseal fractures, for in these cases medullary nailing does not produce stable fixation, but the plate should be used only when conservative measures are ineffective. The author feels that there will be further developments in mechanical fixation of fractures. A careful selection not based on consideration of mechanical or biologic factors alone is necessary in order to avoid failures and incorrect evaluation.

Journal of Endocrinology, London

7:299-378 (Oct.) 1951. Partial Index

- Effect of Thyroidectomy on Reproduction in Female Rabbit. P. L. Krohn.—p. 307.
Induction of Menstrual Bleeding in Amenorrhoeic and Normal Monkeys by Progesterone. P. L. Krohn.—p. 310.
Estimation of Corticosteroid-Like Substances in Human Urine. A. M. Robinson and J. M. Norton.—p. 321.
Ovarian Hypertrophy After Unilateral Hysterectomy. A. M. Mandl and S. Zuckerman.—p. 339.
Action of Glycine on Liver Glycogen of Fasting Mice, Normal and Adrenalectomized. M. F. Lockett and M. M. Evans.—p. 357.
Physiological Factors Affecting Response of Experimental Wound Healing to ACTH. B. E. Clayton and F. T. G. Prunty.—p. 362.

Lancet, London

2:795-844 (Nov. 3) 1951

- Dermatology from the Time of Harvey. A. Gray.—p. 795.
- *Iritis as Presenting Symptom in Ankylosing Spondylitis. M. Q. Birkbeck, W. St. J. Buckler, R. M. Mason and W. S. Tegner.—p. 802.
- Effects of Adrenaline, Noradrenaline, and Methedrine on Renal Circulation During Anaesthesia. H. C. Churchill-Davidson, W. D. Wylie, B. E. Miles and H. E. de Wardener.—p. 803.
- Tuberculin-Neutralising Factor in Patient with Miliary Pulmonary Lesions. A. W. Lees.—p. 805.
- C-Reactive Protein in Chronic Rheumatic Diseases. A. G. S. Hill.—p. 807.
- Annular Pancreas. J. C. N. Wakeley.—p. 811.
- Haemoglobinuria in Typhoid Fever: Report of Two Cases. A. B. Shaw.—p. 813.
- *Two Cases of Ulcerative Colitis Treated with Vitamin B₁₂. G. A. Rail.—p. 816.

Iritis as Presenting Symptom of Ankylosing Spondylitis.—In a series of patients observed by the department of physical medicine at the London Hospital 13 of 148 patients with ankylosing spondylitis had iritis, but Birkbeck and associates feel that it is not generally realized that iritis can be the presenting sign of this syndrome. They recently observed 11 patients who had ankylosing spondylitis when they first sought medical attention for iritis. The authors present brief histories of these patients and say that the iritis associated with ankylosing spondylitis is regarded by ophthalmologists as a nonspecific manifestation of an allergic response. Since the cause of ankylosing spondylitis is not known, and there is no evidence that it is due either to streptococcal or gonococcal infection, the actual cause of the iritis found in this condition is a matter of conjecture. On the other hand, it seems that many patients who seek advice for iritis also have ankylosing spondylitis that is not diagnosed or treated. In view of the powerful therapeutic effects of radiotherapy, cortisone, and corticotropin (ACTH) in ankylosing spondylitis the possibility of co-existent ankylosing spondylitis should be explored in all patients with nonspecific iritis so that such spondylitis can be treated as early as possible.

Vitamin B₁₂ in Ulcerative Colitis.—The two patients reported here had colicky abdominal pains before defecation, tenesmus, and diarrhea with stools containing blood and mucus. Amebic dysentery was suspected, but could not be verified, the repeated search for ova, cysts, and protozoa being negative. Sigmoidoscopy revealed inflammation of the bowel with numerous discrete ulcers and hemorrhagic patches. The diagnosis of ulcerative colitis was arrived at by exclusion, and treatment with vitamin B₁₂ was started, 20 γ being injected daily for from four to seven days and then twice weekly for several weeks. Both patients responded promptly and have remained well for over a year. Many theories of the cause of ulcerative colitis have been propounded, and many remedies have been tried, but none has met with great success. The idea of using a liver extract in ulcerative colitis was first conceived in 1944 when the author noticed the healing effect of high liver diets on residual ulcers in patients with amebiasis. It then seemed that ulcerative colitis might possibly be due to some dietary deficiency. Both patients presented here had, at different times previously, been on diets in many ways inadequate as compared with their customary diets.

Medical Journal of Australia, Sydney

2:417-452 (Sept. 29) 1951. Partial Index

- Further Revision of Dermatomes. J. H. Young.—p. 425.
- Some Observations on Treatment of Otitis Externa and Otitis Media. W. E. David.—p. 427.
- Pregnancy Toxaemia. W. F. Joynt.—p. 434.

2:453-484 (Oct. 6) 1951

- Pancreatitis at Royal North Shore Hospital of Sydney from 1925 to 1950. T. F. Rose.—p. 453.
- Venous Occlusion Plethysmography: II. Aid to Diagnosis and Management of Peripheral Vascular Disease. A. J. Barnett.—p. 458.
- Problem of Simple Goitre. F. F. Rundle.—p. 464.
- *Abdominal Migraine: Report of Case. D. W. Piper.—p. 468.
- Case of Hemiparesis Following Cut Throat. J. B. Nally.—p. 469.

Abdominal Migraine.—Migraine, in its protean forms, is a symptom complex usually dominated by headache. Abdominal migraine is one of the rarest migrainous variants. The case reported here began as so-called cyclical vomiting in childhood, and the symptoms, persisting into adult life, were characteristic

of abdominal migraine. The patient, now 16 years old, had had attacks of vomiting since the age of 3. The attacks of vomiting lasted about one week and then did not occur for one or two weeks. This cycle was repeated for two to six months, and then she did not vomit again for about two years. Her family history revealed that her two brothers and father had migraine. Before her admission to hospital the therapeutic effect of ergotamine tartrate (gynergen®) was tried, and on three occasions it stopped the attacks in a few hours, although they usually lasted for one week. Electroencephalographic studies disclosed minor abnormalities. Commenting on this case, Piper cites the opinions of other authors and says that there appears to be no clear dividing line between cyclical vomiting of childhood and the abdominal variant of migraine. The functional pathology of abdominal migraine is obscure. Moore believed that the abdominal symptoms are due to discharges arising in cortical areas 6, 5, and 3 of Brodmann, or in the diencephalon, or in both, which produce abnormal motility of the intestinal tract with resultant pain. He urged that it be called abdominal epilepsy and not abdominal migraine.

Minerva Medica, Turin

42:219-242 (Aug. 25) 1951. Partial Index

- *Therapeutic Experiments with Visammin in Coronary Disease. F. I. Giuseppe.—p. 219.
- Presence of Mast Cells in Bone Marrow: Relationships Between Mast Cells and Heparinic Activity of Plasma in Pathogenesis of Thrombosis and Spontaneous Hemorrhage. P. Meneghini.—p. 223.
- Occupational Dermatitis Due to Streptomycin. A. Chierici.—p. 230.

Visammin in Coronary Disease.—Visammin (khellin) was given to 2 patients with myocardial infarction and to 14 patients with angina of effort, two of whom had recently suffered myocardial infarction. A daily dose of 120 mg. divided into two 40 mg. tablets and one parenteral injection of 40 mg. was given for 7 to 10 days. In some mild cases the dose of choice seemed to be two 40 mg. tablets given daily after meals. Treatment was continued for 10 to 20 days. Anginal pain and attacks receded in 10 patients, including the 2 with myocardial infarction. Side effects were pronounced in two patients in whom treatment had to be discontinued on the 4th and the 19th day respectively. In one patient, who had tolerated parenteral administration of 400 mg. of visammin, one tablet of 40 mg. caused severe gastric disturbances, and the treatment was suspended. Results could not be evaluated in one patient. The use of this powerful vasodilator drug in coronary disease is limited by the side-effects that increase with larger and repeated doses.

Presse Médicale, Paris

59:1321-1340 (Oct. 13) 1951

- *Treatment of Syphilitic Aortitis with Penicillin. C. Lian, R. Nedel and A. Cassimatis.—p. 1321.
- *Causes of Failures in Surgical Treatment of Protruded Intervertebral Disk. A. Sicard.—p. 1323.
- Essential Polycythemia and Serum Iron. M. Tubiana and F. Schapira.—p. 1324.

Penicillin in Syphilitic Aortitis.—Penicillin was administered to 24 patients with syphilitic aortitis, including 19 with aortic insufficiency, 2 with syphilitic aneurysm, and 3 with aortic insufficiency and aneurysm. Six intramuscular injections of an aqueous solution of the antibiotic were given daily for 10 to 15 days. The initial dose varied from 200,000 units to 1,000,000 units and the total dose of one course of treatment varied from 3,000,000 to 15,000,000 units. Several patients were given repeated courses of treatment. Two patients died, one on the third day of penicillin treatment and the other on the third day after termination of treatment, but neither death could be attributed to the penicillin therapy. Except for a temporary febrile reaction in three patients and an urticarial eruption in one, the treatment was well tolerated. The Herxheimer reaction did not occur in any patient. There was pronounced and rapid relief of substernal pain. The effect of the drug on cardiac decompensation was less evident because of the combined administration of cardiotonic agents, but several patients were definitely benefited. Although undesirable effects of penicillin therapy have been observed only in exceptional cases, the authors consider it advisable first to treat patients with syphilitic aortitis as non-

syphilitic patients with angina pectoris or cardiac decompensation. Only when this treatment fails or when the results appear to be inadequate should penicillin therapy be used and combined with administration of cardiotonic agents, diuretics, and dietetic treatment. As a precautionary measure, a few injections of mercuric cyanide should be given before penicillin is instituted. The minimum daily dose of penicillin should be 500,000 units, and it may be increased to 1,000,000 units daily for at least two weeks, but continued for three to four weeks if required. It should be followed by a one-month course of treatment with mercuric cyanide and, in the absence of renal insufficiency, by another one-month course of treatment with bismuth. This three month-treatment should be repeated three or four times during one year until the patient's serum becomes negative and there is pronounced improvement of the cardiovascular disturbances.

Failure in Surgery for Protruded Intervertebral Disk.—Of 842 patients with protruded intervertebral disk operated on by the author, 34 (4%) were not benefited. Repeated surgical intervention in the 34 patients and in an additional 14 patients operated on by other surgeons made it possible to determine the causes of the failure of the first intervention. In 8 patients the protruded disk was not detected because of an error in locating the involved disk, deficient exploration, or inadequate exposure. Additional protrusion at the level of the subjacent disk in two cases and contralateral protrusion in one case were not detected, but protrusions of these types are rare. Inadequate removal of the protruded portions of the intervertebral disk was observed in six cases, and the compressed nerve root had been injured in the course of its liberation in five cases; faulty technique is to be considered responsible for therapeutic failure in these cases as well as in those of secondary arachnoiditis resulting from opening the dura mater and from operative injury of the cauda equina. This type of therapeutic failure is avoidable with perfect surgical management. In three cases pain in the sacral region radiating along the sciatic nerve resulted from the persistence of iodized oil in the dural sac in contact with the nerve roots; the use of this contrast medium is a method of exploration that should be employed only in exceptional cases. Secondary arthrosis associated with permanent lumbosacral pain was revealed in 23 cases, but may be prevented by performing complementary arthrodesis, particularly in cases in which pronounced arthrosis may be present before the surgical intervention and in those with a temporary abnormal condition of the joint. With well-defined indications for surgical treatment and with correct technique, the incidence of surgical failure in treatment of protruded intervertebral disk should be lowered, but if pain persists the operation should be repeated.

59:1341-1360 (Oct. 17) 1951. Partial Index

Submicroscopic Structure and Functioning of Connective Tissue. A. Pollicard.—p. 1341.

*Combined Hormone-Salicylate Treatment of Rheumatic Fever. M. Janbon, L. Bertrand, J. Salvaing and R. Labauge.—p. 1344.

Hormone-Salicylate Treatment of Rheumatic Fever.—The use of a short, intensive course of cortisone therapy followed by a longer course of salicylate therapy proved highly effective in 18 cases of rheumatic fever treated by the authors. Twelve cases were first attacks and six were relapses; the heart, or at least the pericardium, was affected in all. The antirheumatic action of sodium salicylate is similar to that of corticotropin (ACTH) and cortisone, but results of hormone treatment are more rapid and intense than of salicylate treatment. Combination of the two agents reduces the disadvantages arising from exclusive use of either medication. Salicylate dosage is highly variable; time spent in determining the proper dose represents a serious danger when speed is needed to avert cardiac damage. Hemorrhage, ketosis, and similar complications usually occur while salicylate treatment is being started. The initial use of cortisone obviates these difficulties, and the subsequent use of salicylates makes unnecessary prolonged cortisone therapy with its attendant risk. In the combined treatment cortisone is used until fever subsides, usually on the third or fourth day. Adults are usually given 300 to 400 mg. in four injections during the first day, 200 to 300 mg. in two injections the second day, and a single injection of

100 to 200 mg. on the third and sometimes the fourth day. Children receive 150 to 200 mg. the first day, with other doses in proportion. Clinical stabilization follows discontinuation of cortisone for about five days. Unless salicylate treatment is instituted, the temperature rises abruptly on the seventh day. Salicylate dosage should be moderate at first, when cortisone is discontinued, and should be increased gradually, with special attention to the critical seventh day. The authors use sodium gentisate orally, the average adult dose being 14 gm. daily in fractional doses; and sodium salicylate intravenously, 4 gm. in two injections. The amount of cortisone required to reduce the fever is a guide to the amount of salicylate needed. Alterations in blood sedimentation rate, fibrinogen, and tests of protein imbalance, especially the Weltmann coagulation column, serve as guides during treatment and indicate when it may be discontinued. This should be preceded by gradual reduction of medication. Salicylate treatment of the authors' patients never exceeded one month. General symptoms and signs responded rapidly to treatment. The response of the heart in the patients undergoing their first attack depended on the time of administration of cortisone. When it was started by the 12th day of the disease, development of endocarditis was averted; when it was started about the 15th day, existing aortic and mitral insufficiency disappeared; but when it was postponed until after the 20th day, existing endocarditis was not improved, and, at best, damage was arrested. The authors believe that hormone treatment is the best preventive of rheumatic carditis and should be given in all cases of acute rheumatic fever. The method of choice is to combine it with prolonged salicylate treatment.

Progrès Médical, Paris

79:513-544 (Oct. 24) 1951

*Tobacco Test in Electrocardiographic Diagnosis of Angina Pectoris. P. Bardin and T. Doliopoulos.—p. 515.

Disturbances and Diseases of Growth. R. Liège.—p. 516.

Management of Bone Metastases. J. S. Bourdin.—p. 523.

Tobacco Test in Diagnosis of Angina Pectoris.—Electrocardiograms were taken of 21 men between the ages of 40 and 73 with thoracic pain suspected of being anginal. In addition to the three unipolar limb leads, six precordial leads were used. In 18 patients the electrocardiograms showed normal function. The electrocardiograms of the remaining three patients showed a negative T wave in the unipolar limb leads as well as in the precordial leads. The patients then were asked to smoke two cigarettes and the electrocardiograms were repeated 5 to 10 minutes later. One-fourth of the patients did not "inhale." In 19 patients, including the three with the coronary changes, the electrocardiograms taken after the tobacco test did not show any changes when compared with those taken before the tobacco test. Of the electrocardiograms of the remaining two patients, one revealed reversal in the direction of the T wave, and the other a diphasic T wave in leads V₂, V₃, and V₄. These changes were within the compass of the atypical changes associated with angina pectoris. According to the reports of other workers these changes may be observed likewise in physiological conditions after tobacco smoking. The tobacco test did not precipitate pain in any of the patients tested. The tobacco test does not seem to be a suitable substitute for the anoxemia or exertion tests in diagnosis of angina pectoris.

Riforma Medica, Naples

65:973-996 (Sept. 8) 1951. Partial Index

Studies on Pathogenesis of Recurring Malaria: Observations Based on Recent Discoveries of Biologic Cycle of the Parasite. F. Conti and R. Monaco.—p. 974.

*Adjuvant Therapy in Abdominal Surgical Interventions: Use of Marbadal in 50 Cases of Peritonitis. C. Tangari.—p. 982.

"Marfanil" Sulfathiourate in Abdominal Surgical Intervention.—*p*-aminomethylbenzene sulfonamide ("marfanil") sulfathiourate was used as an antibacterial adjuvant in surgical intervention for severe intraperitoneal infections, including 30 cases of acute gangrenous and perforating appendicitis, 10 cases of perforating duodenal ulcers, 5 cases of perforating and 5 cases of diffuse peritonitis due to typhoid. Dectomy was followed by cleansing of the

that was then sprinkled with 10 gm. of "marfanil" sulfathiourate. An additional 5 gm. of the powder was spread subcutaneously. Gastric resection and suture of a perforating ulcer was followed by the same procedure. Three patients with diffuse purulent peritonitis admitted to the hospital in desperate condition 48 and 60 hours after the intestinal perforation died. Complications did not occur in the remaining 47 in whom the postoperative course was short. The drug exerted a beneficial effect on peristalsis.

Schweizerische medizinische Wochenschrift, Basel

81:985-1028 (Oct. 13) 1951. Partial Index

- Effect of Androgens on the Metabolism. C. D. Kochakian.—p. 985.
 Action of Progesterone on Cutaneous Thermal Reaction of Menopausal Women. R. Borth, A. Heltai and H. de Watteville.—p. 991.
 *Treatment of Osteoporosis with Sex Hormones. A. Labhart and A. Schüpbach.—p. 992.
 Mode of Administration of Steroid Hormones and Its Therapeutic Importance. C. Hamburger.—p. 995.
 *Hormone Therapy in Diseases of the Prostate. E. Wildbolz.—p. 999.

Treatment of Osteoporosis with Sex Hormones.—There is a discrepancy between the roentgenologic and pathologic concepts of osteoporosis. To the roentgenologist this term frequently signifies merely a calcium deficiency of the bone, although he realizes that this calcium deficiency may be caused by such diverse disorders as Recklinghausen's disease (osteitis fibrosa cystica), osteomalacia, and true anatomic osteoporosis. These three entities are characterized also by the same clinical triad: bone deformities, increased tendency to fracture, and bone pains. Recklinghausen's disease and osteomalacia can usually be differentiated on the basis of laboratory data, but the laboratory provides no information in true osteoporosis, with which this report is concerned. Osteoporosis is a bone atrophy in which the constructive component fails but destruction continues. Two factors are involved in the atrophy: (1) lack of protein material for the build-up of the basic protoplasmatic substance of bone, and (2) defective function of the osteoblasts. After briefly discussing the types of osteoporosis in which a deficiency in serum proteins plays a part (starvation, pregnancy, and nephrosis) and the so-called inactivity osteoporosis, brought about by deficient activity of the osteoblasts during immobilization (paralysis or plaster cast), the authors discuss the osteoporosis observed in the aged. They stress the role of hormone deficiencies and show that administration of sex hormones is of great importance in treatment of this form of osteoporosis. Both estrogens and androgens are used. They quote Albright's suggested dosage for therapy with sex hormones and describe their own modification of the hormone therapy. They also mention possible adverse effects, such as cancerigenic effects, and how they might be minimized.

Hormone Therapy in Diseases of the Prostate.—Wildbolz discusses the present treatment of prostatitis, of hypertrophy of the prostate, and of carcinoma of the prostate, particularly the use of hormones and of castration. He recommends the use of the male sex hormones chiefly for chronic, nonspecific prostatitis. The estrogens, female sex hormones, are helpful in hypertrophy and carcinoma of the prostate. He also explains when he resorts to surgical treatment of the prostate. He says that he resorts to castration for carcinoma of the prostate when the estrogens have lost their efficacy or when it seems desirable to intensify rapidly the action of the estrogens, as well as in neglected patients who do not take the estrogenic preparations.

81:1069-1096 (Nov. 3) 1951. Partial Index

- *Differential Diagnosis of Nonparalytic Poliomyelitis. G. Fanconi.—p. 1070.
 Modern Concept of Allergy: Difficulties It Creates for the Dermatologist. P. Robert.—p. 1075.
 Question of Pulmonary Changes After Bronchography with Contrast Mediums Containing Carboxymethylcellulose. A. Werthemann and W. Vischer.—p. 1077.
 Development of Pulmonary Tuberculosis After Pleurisy. A. Wernli-Haessig.—p. 1080.

Differential Diagnosis of Poliomyelitis.—Fanconi points out that American investigators have largely rejected the so-called meningitic phase of poliomyelitis, arguing that it is really only a secondary accompaniment of the encephalomyelitis. Rigidity of neck and back is ascribed to muscular spasms rather than to

meningitis. Fanconi believes, however, that it is helpful for differential diagnosis to distinguish between a meningitic and an adynamic (asthenic) phase during the preparalytic stage of poliomyelitis. If symptoms of an adynamic phase can be demonstrated the diagnosis of poliomyelitis is quite certain. He regards the following symptoms as characteristic of the adynamic, asthenic phase: (1) general muscular weakness recognizable as a weak hand pressure; (2) flaccidity of the neck if the head suddenly lifted up; (3) shifting of the umbilicus if the child ordered to sit up; (4) the fact that the reflexes become weak or show disparity after having been intensified during the meningitic phase; in some cases the patellar tendon reflex becomes weaker or disappears entirely, whereas the patello-adductor reflex is preserved or even intensified; (5) the presence of a coarse tremor; and (6) muscular spasms. If the symptoms do not advance beyond the meningitic stage, then it becomes necessary to rule out a number of nonsuppurating meningitides, such as tuberculous, meningococcal, or influenzal meningitis, as well as various nonpoliomyelitic types of virus meningitis. The differentiation between poliomyelitic meningitis and other types of meningitis becomes increasingly difficult as more and more meningotropic viruses are discovered and the concept of the etiology of poliomyelitis becomes more and more indefinite with discovery of new Cocksackie viruses resembling that of poliomyelitis. The author discusses the cerebrospinal fluid changes of various infections likely to produce meningitic symptoms and then advances a theory to explain the different stages of many neuropathic infections. He also shows that analysis of the cerebrospinal fluid often fails to clarify the diagnosis of poliomyelitis, and that many infections are at times likely to produce meningitis and are thus likely to cause mistaken diagnoses.

Semaine des Hôpitaux de Paris

27:3105-3152 (Oct. 26) 1951. Partial Index

- Study of Venous Pressure, Circulatory Velocity and Diuresis in 18 Cases of Female Obesity. M. Albeaux-Fernet, J. Berton, R. Cauvin, J. R. M. Franckson.—p. 3105.
 Significance of Inorganic Serum Phosphorus Level for Testing Pituitary Somatotrophic Hormone Activity. J. Berton and J. Robert.—p. 3111.
 *Therapeutic Action of Corticotropin (ACTH) and Cortisone in Selected Endocrine Disorders. Albeaux-Fernet.—p. 3114.

Corticotropin and Cortisone in Endocrine Disorders.—This is a general review of recent reports of results obtained with corticotropin (ACTH) and cortisone in treatment of endocrine disorders. 1. There was improvement in patients with secondary adrenal insufficiency; in addition a small number of patients with congenital adrenal hyperplasia showed at least temporary improvement. 2. Patients with hyperthyroidism were improved probably through pituitary blocking. Exophthalmos was not reduced, but in one of the author's patients slight diminution of the conjunctival hyperemia, notable improvement of visual acuity, and considerable improvement in the arteries of the fundus resulted from bilateral retrobulbar injections of 5 mg. of cortisone every second day for 20 days. 3. The number of patients with ovarian disorders treated with these drugs has been too small to permit definite conclusions. 4. As a result of treatment with corticotropin and cortisone is contraindicated in patients with disorders of carbohydrate metabolism, but antagonistic action of corticotropin to insulin proved beneficial in children with spontaneous idiopathic (non-Addisonian) hypoglycemia. 5. According to American authors, corticotropin and cortisone are definitely indicated in treatment of pituitary insufficiency, and assist in determining the diagnosis and prognosis as well.

Tidsskrift for Den Norske Laegeforening, Oslo

71:611-632 (Oct. 1) 1951. Partial Index

- *Secondary Virus Infection in Eczema (Kaposi's Varicelliform Eruption). O. Gilje.—p. 611.
 Acute Porphyria in Family from Northern Norway. P. F. Iversen.—p. 616.
 Diagnosis of Heart Disease by Industrial Physician. C. Müller.—p. 616.

Secondary Virus Infection in Eczema (Kaposi's Varicelliform Eruption).—Six cases of pruriginous eczema complicated by secondary infection with herpes simplex virus are reported. One occurred in a man aged 20, and five occurred in infants. Fol-

ing aggravation of the eczema a vesicular eruption appeared suddenly, accompanied by elevation of temperature and systemic symptoms. In five cases there was swelling of cervical lymph nodes, and in one case, swelling of axillary nodes. The disturbance lasted about a week. Treatment with aureomycin in four cases gave excellent results. The introduction of aureomycin therapy will probably improve the prognosis in Kaposi's varicelliform eruption, which has hitherto been regarded as less favorable. In differential diagnosis eczema vaccinatum is mainly to be considered. Here the exanthem presents a more monomorphic picture, and the history is helpful in diagnosis. If the patient has been vaccinated recently or been in contact with recently vaccinated persons, the possibility of eczema vaccinatum should be borne in mind. If on the other hand, as in three of the cases described, there is a near-by source of infection with herpes simplex this suggests Kaposi's varicelliform eruption.

Ugeskrift for Laeger, Copenhagen

113:1177-1214 (Sept. 6) 1951. Partial Index

- *387 Electroshock Treatments with Decamethonium Bromide (C_{10} "Synacur"). J. Kaldan.—p. 1183.
Treatment of Narcotic Intoxications. E. Nilsson.—p. 1185.
Mental Hygiene and Practising Physician. J. Wagner Smitt.—p. 1193.

387 Electroshock Treatments with Decamethonium Bromide (C_{10} "Synacur").—Kaldan gave 387 electroshock treatments with the synthetic preparation decamethonium (C_{10} "synacur") as the relaxing agent. The usual psychiatric indications for shock treatment were followed. No allergic phenomena were observed in connection with the treatment. The effect of the drug disappeared quickly. Respiratory complications were readily overcome by artificial respiration with oxygen. No other complications were seen. The author suggests that perhaps preparatory muscle-relaxants should be given with all shock therapy if the new synthetic preparations fulfill their promise.

113:1297-1334 (Sept. 27) 1951. Partial Index

- Case of Macrocytic Goat's Milk Anemia Successfully Treated with Vitamin B₁₂. E. Rud.—p. 1301.
*Duration of Life in Cases of Chronic Leukemia in Childhood. P. Andersen and J. Kringelbach.—p. 1304.
Vanadium Intoxication from Cleaning Oil-Burning Boilers. J. Frost.—p. 1309.
Morphine Intoxication After Therapeutic Morphine Doses. H. Hove.—p. 1312.
Monofilament Nylon for Skin Sutures. E. T. Madsen.—p. 1314.

Duration of Life in Chronic Leukemia.—In most cases of leukemia in childhood the course is acute. Chronic myeloid leukemia is characterized by insidious onset, protracted course, marked enlargement of the spleen, no or slight peripheral adenitis, and pronounced increase of cell count in the peripheral blood. In only 2 of 71 cases of myeloid leukemia in children under 15 treated in Denmark from 1942 to 1949 was the course chronic; one patient lived about two and a half years after the probable start of the disease, and the other lived more than four and a half years.

113:1335-1364 (Oct. 4) 1951. Partial Index

- *Hexamethonium Bromide Treatment of Essential Hypertension. P. Bechgaard, T. Iversen and A. L. Nielsen.—p. 1335.
Eosinophilia Developed During Administration of Corticotropin (ACTH). A. Videbaek.—p. 1345.
Effect of Corticotropin (ACTH) Treatment on Otosclerosis and Adhesive Otitis. N. Riskær.—p. 1349.
Case of Temporal Arteritis Treated with Corticotropin (ACTH). H. P. Østergaard Kristensen.—p. 1353.

Hexamethonium Bromide Treatment of Essential Hypertension.—Hexamethonium bromide was used in the treatment of 12 hypertensive patients aged from 43 to 67. If the blood pressure did not fall with doses up to 4 gm. daily, the treatment was discontinued. In seven cases there was a definite fall in blood pressure, accompanied by relief of headache and dizziness in four cases. In one of these cases treatment was discontinued because of cerebral thrombosis, and in two cases because the patients did not feel well. In three cases there were marked side-effects in the form of postural hypotension. In six cases the blood pressure rose when the treatment was discontinued. In one instance, in a

45-year-old man with malignant hypertension, marked papilledema, and impairment of vision, treatment with hexamethonium bromide and salt-poor diet resulted in definite and rapid improvement. The blood pressure remained normal for five weeks after the cessation of treatment and was kept low for nine months after the start of treatment by periodic administration of hexamethonium bromide supplemented with salt-poor diet; the patient feels well. The authors conclude that hexamethonium bromide is hardly to be recommended in treatment of essential hypertension in older patients but may be tried in graver forms of hypertension in younger patients.

Wiener medizinische Wochenschrift, Vienna

101:721-744 (Sept. 22) 1951

- Law of Maintenance of Living Substance. E. Santo and H. P. Rusch.—p. 725.
*BCG Allergy and Infection Allergy. O. Ruziczka.—p. 734.

BCG Allergy and Infection Allergy.—Three and a half months after BCG vaccination, Pirquet's scarification tests or tuberculin patch tests were performed on 1,467 school children between the ages of 6 and 14. The scarification tests were made with BCG tuberculin and with old tuberculin on symmetrical spots of the forearms, and the patch tests were made with BCG tuberculin and old tuberculin on symmetrical spots of the chest. The BCG tuberculin was concentrated by evaporation to $\frac{1}{3}$ of its original volume, and the old tuberculin was concentrated to $\frac{1}{10}$ of its original volume, so that both tuberculins were lethal in the same dose for the guinea pig and gave the same cutaneous reactions. The old tuberculin was sterilized for four hours at 100 C, while the BCG tuberculin was not sterilized. In 80 to 90% of the children, BCG allergy was definitely demonstrated by the extent, the color, and rapid course of the reaction to the scarification tests and the patch tests performed simultaneously with old tuberculin and BCG tuberculin of equivalent potency. Thus the objection against BCG vaccination that the valuable tuberculin diagnosis of tuberculous infection had been lost was invalidated. In children with active tuberculosis the reaction to both the BCG tuberculin and the old tuberculin is extensive, dark red with pronounced infiltration, and prolonged. The differences in extent, color, infiltration, and duration of the individual reactions make clinical differentiation of allergy caused by BCG vaccination from active tuberculous disease possible in many children. The distinction cannot be made in children with tuberculous meningitis, milary pulmonary tuberculosis, tuberculous pleuritis, and severe pulmonary tuberculosis. Investigations of results of the two tuberculin tests in patients with inactive forms of tuberculosis have not been concluded. It is suggested that physicians, nurses, and persons in other occupations particularly exposed to the risk of tuberculosis infection be subjected to tests with both tuberculins in order to obtain important comparison values for later evaluation of virulent superinfection. Pirquet's scarification test seems to be particularly suitable for this purpose.

101:833-852 (Nov. 3) 1951

- *Therapy of Purulent Meningitis. F. Mayr and A. Steinbäcker.—p. 833.
Reticuloendothelial Supporting Tissue of Waldeyer's Tonsillar Ring as Point of Origin of Systemic Diseases (Lymphogranuloma). E. Bauer.—p. 835.
Ureterocele Prolapsed into Vulva. K. Menhofer.—p. 839.
Modern Antibiotics in Properly Directed Antibacterial Therapy of Infections of Urine. H. Meuser and H. Haschek.—p. 840.

Therapy of Purulent Meningitis.—Seven patients with severe purulent meningitis were treated according to the following method: the patient was placed on an operating table that could be elevated and lowered at both ends. After intravenous injection of 0.125 mg. of strophanthin and dextrose and induction of anesthesia with 60 mg. of thiopental sodium in 50 cc. of water, lumbar puncture followed by suboccipital puncture were performed by different physicians. When cerebrospinal fluid flowed spontaneously from the lumbar needle, the foot-end of the operating table was lowered about 30 degrees and Ringer's solution was introduced suboccipitally. Cerebrospinal fluid usually escaped more rapidly after the introduction of the first 10 to 20 cc. of the irrigation fluid. If the cerebrospinal fluid

did not flow spontaneously from the lumbar needle, irrigation was carried out in the lumbo-occipital direction. After the passage of 200 cc. of Ringer's solution the head-end of the operating table was elevated about 30 to 40 degrees above the horizontal line; by subarachnoid injection of about 20 to 30 cc. of air, an additional 40 cc. of cerebrospinal fluid was allowed to escape. The lumbar puncture needle was left in place while the suboccipital puncture needle was pulled back behind the posterior cervical ligament, and then again advanced slowly with a syringe filled with air until diminished resistance permitted injection of the air into the subdural space. With the puncture needle in the correct position, the cerebrospinal fluid no longer flowed. Then 20,000 to 25,000 units of penicillin were injected into the subdural space, and the suboccipital puncture needle was withdrawn. Antibiotics were administered through the lumbar puncture needle, which then was withdrawn. The patient was then placed in horizontal position with the head lowered, so that the air in the subdural space could escape toward the cervical portion of the vertebral column and the penicillin solution could irrigate the remaining subdural space. Undesirable side-effects were prevented by control of respiration, pulse, blood pressure, and cutaneous blood flow. The main advantage of this method is that the penicillin contacts the network of the pia-arachnoid, as revealed by the yellow color of the cerebrospinal fluid. The resistance and general condition of the patient were favorably influenced by the injected air. Within four to seven days the patients were improved considerably, and all survived. Despite the small number of patients reported on, this method of treatment is to be considered promising.

Zeitschrift f. Geburtshilfe u. Gynäkologie, Stuttgart

135:121-236 (No. 2) 1951. Partial Index

- Analgesia During Delivery. E. Fauvet.—p. 149.
 Pregnancy Toxicoses: Presence of Antidiuretic and Vasopressor Substances in Blood and Urine and Their Importance for Symptomatology. F. Hoffmann.—p. 169.
 *Modification by Rutin of Capillary Resistance and Capillary Permeability During Pregnancy. H. Burger.—p. 182.
 Differentiation of Serum Proteins of Pregnant Women, Nursing Infants and Premature Infants by Means of Electrophoresis. P. Pfau.—p. 194.
 Changes in Serum Proteins During Hyperemesis Gravidarum: Relation to Instability Reaction. V. Friedberg.—p. 214.

Influence of Rutin on Capillary Permeability During Pregnancy.

In order to ascertain whether rutin influences capillary permeability during pregnancy, Burger first made experiments on healthy pregnant women and found that pregnancy is usually accompanied by a reduction in capillary resistance and an increase in capillary permeability for water and protein. He also found that impairment in permeability plays a part in the pathogenesis of eclamptic disorders. Vitamin P in the form of rutin normalizes the impaired peripheral exchange mechanisms, and consequently its use might prove valuable during pregnancy. The mode of action of rutin is discussed.

Zentralblatt für Chirurgie, Leipzig

76:1297-1360 (No. 19) 1951. Partial Index

- *Cancer of Breast: Pathologic Aspects and Therapy. F. Mörl.—p. 1298.
 *Evaluation of Sternal Puncture in Carcinoma of Breast. B. Winckelmann.—p. 1308.
 Surgical Treatment of Biliary Tract. F. Bordsch.—p. 1310.
 Gas Gangrene of Liver. H. Griessmann.—p. 1316.
 Treatment of Postoperative Duodenal Fistula. M. Zwicker.—p. 1317.
 Ileus of Small Intestine in Case of Closed Perforation of Meckel's Diverticulum. K. H. Köhler.—p. 1320.
 Differential Diagnosis of Terminal Ileitis. M. Kinzler.—p. 1322.

Cancer of Breast.—Mörl emphasizes the importance of the retrosternal lymph nodes in dissemination of cancer of the breast. In the past emphasis was placed largely on the axillary and infraclavicular group of lymph nodes until the Swiss roentgenologist, Walther, and the British surgeon, Gordon Taylor, stressed the importance of the retrosternal chain of lymph nodes. Mörl has studied these lymph nodes in cases of carcinoma of the breast and points out that the retrosternal chain of lymph nodes belongs to the regional lymph node system of the breast just as much as the axillary and the infraclavicular chains. Its significance for the lymphogenous metastasis of breast cancer

is almost as great as that of the other two groups of lymph nodes, that is, it may contain metastatic lesions when the other two chains are still free. Even carcinoma in the upper external quadrants (the most frequent localization) occasionally metastasizes to the more distant retrosternal lymph nodes, with the possibility of direct spread of the carcinoma to the pleura, giving rise to carcinomatous pleuritis. If the endothoracic (retrosternal) lymph node chain is not removed at operation, it may become the point of origin for distant metastases. The operation for breast cancer in which this chain is not removed cannot be regarded as radical.

Sternal Puncture in Carcinoma of Breast.—Winckelmann examined the sternal marrow in 50 patients with histologically verified carcinoma of the breast and found carcinoma cells in 21 of the patients. A table that classifies the patients according to the histologic type of their carcinoma indicates that although in some forms the incidence of carcinoma cells in the sternal marrow is higher than in others, the type does not determine sternal metastasis. At any rate, it should be realized that the absence of carcinoma cells in the sternal marrow does not exclude existence of a malignant lesion, but their presence corroborates the diagnosis of cancer.

76:1361-1440 (No. 20) 1951. Partial Index

- *Congenital Pulmonary Arteriovenous Fistula and Its Surgical Treatment. E. Derra.—p. 1362.
 Results of Endotracheal Anesthesia with Curare. L. Zürn.—p. 1368.
 Intravenous Drip-Anesthesia with Barbiturates. H. Grewe and K. Kremer.—p. 1382.
 Familial Occurrence of Multiple Basal Cell Tumors of Scalp (So-Called Spiegler's Endothelioma). E. Hagemann.—p. 1388.

Congenital Pulmonary Arteriovenous Fistula.—The occurrence of congenital pulmonary arteriovenous fistula is reported in a woman aged 27. Cyanosis and weakness were observed for the first time following measles when the patient was 9 years old. Headache, cough, and expectoration became frequent. Attacks of faintness and temporary stiffness of the left side occurred four to five times at the age of 14. Clubbing of the digits became persistent from the early school years onward. Later polycythemia was demonstrated, and diagnosis of chronic circulatory and heart disease was made. During the three years preceding surgical intervention, the patient's condition became worse, with increased cyanosis of the face and feet, pain in the area of the heart, and severe palpitation. Temporary paresthesia of the left arm occurred, there was loss of appetite and hematemesis, considerable increase of fluid in the vessels of the fundus oculi with hyperemic optic papilla, pronounced vascularization of the palate and of the posterior pharyngeal wall, and telangiectasia of the nasopharyngeal mucous membrane but not of the face. The hemoglobin level was about 135% of normal, there were 7,500,000 erythrocytes, and the hematocrit values were about 81. A palm-sized area of dullness was noted over the posterior, inferior aspect of the right side of the chest adjacent to the vertebral column, with a superimposed loud systolic murmur on inspiration that was less distinct on expiration, while the respiratory sounds were normal and the heart did not seem to be enlarged. Roentgenograms of the chest showed intensive, somewhat cloudy, opacity in the right lung field, extending to the hilus. On the basis of this evidence diagnosis of pulmonary arteriovenous fistula was not difficult. Lobectomy was performed because of localization of the process in the right lower lobe. Cyanosis subsided permanently, and hematemesis did not recur. Within four weeks after the operation the hemoglobin was reduced to 102% and the number of erythrocytes to 5,100,000. Spirographic deficiency and respiratory insufficiency during rest could no longer be demonstrated. The vital capacity was still reduced to 1.4 liters and the respiratory threshold value to 28 liters, but these manifestations of reduced respiratory reserve are common sequelae of lobectomy. Because of the unfavorable prognosis of pulmonary arteriovenous fistula, there is no other treatment but surgical. Under the most favorable conditions local excision may be curative, but as a rule lobectomy or pneumonectomy is required. These are curative provided there are not multiple fistulas in both lungs. Further experience is required for the evaluation of surgical intervention limited to ligation of the corresponding pulmonary artery.

BOOK REVIEWS

Visceral Innervation and Its Relation to Personality. By Albert Kuntz, M.D., Ph.D., Professor of Anatomy, St. Louis University School of Medicine, St. Louis. Publication number 115, American Lecture Series, monograph in American Lectures in Anatomy. Edited by Otto F. Kampmeier, M.D., Ph.D., Professor of Anatomy and Head of Department, University of Illinois College of Medicine, Chicago. Cloth. \$4.50. Pp. 152, with 31 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, 1951.

This book presents a concise, objective account of the many facts now known about the nervous connections between the viscera and the central nervous system. The major divisions are devoted to (1) the general plan of somatic and visceral innervation, (2) the autonomic nerves, (3) reflex and integrating centers and central conduction pathways concerned in visceral functions, (4) general physiology, including the chemical mediation of nervous impulses and the metabolic influences thereof, (5) innervation of specific viscera, and (6) visceral neural factors in personality.

The first five sections will be welcomed by students of anatomy as an up-to-date and authoritative summary of a difficult subject, useful primarily to those who are already well oriented in neuroanatomy and neurophysiology. As contributions to the technical literature of medicine they deserve high praise. They are, unfortunately, not exciting to read, and one looks forward to the concluding section in the hope that some vivid writing may suggest new insights into human foibles. One would like to understand why some persons react to stress with emesis, others with globus hystericus, others with gastric ulcer, and still others with enuresis. One would like to know what other individual peculiarities may be correlated with the so-called emotional bladder, and whether the urinary difficulties of aging men ever occur in the absence of demonstrable lesions. The inability of some persons to feel hunger pains stands in contrast to the irritability of others in the presence of visceral tensions of various kinds. These phenomena, with many others of great practical importance, involve connections between brain and viscera, and their general explanation lies in the anatomic facts presented in the first five sections of this book, but the immense diversity of human behavior is illuminated not so much by the consideration of what is typical for the race as by the appreciation of what is distinctive for the individual. Certainly the diversity of human personalities is not suggested by refurbishing the simple old ideas (page 119) about sympathicotonia and vagotonia; there was at least the possibility of greater variety in the medieval classification into phlegmatic, sanguine, splenic, and atrabilious types. Since the present treatment of this interesting subject is so cursory, it is to be hoped that the author will undertake a more circumstantial study of it in the future.

The book is well illustrated, faultlessly printed, and has a good bibliography and index.

Surgical Measures in Hypertension. By Reginald H. Smithwick, M.D., Professor of Surgery and Chairman of Department of Surgery, Boston University, School of Medicine, Boston. Publication number 61, American Lecture Series, monograph in American Lectures in Surgery. Edited by Michael De Bakey, M.D., Professor of Surgery and Chairman of Department of Surgery, Baylor University College of Medicine, Houston, Texas, and R. Glen Spurling, M.D., Clinical Professor of Surgery, University of Louisville, Louisville, Kentucky. Cloth. \$3. Pp. 95, with 37 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, 1951.

This monograph briefly reviews the surgical measures employed in the treatment of hypertension, emphasizing the author's preference for a limited form of splanchicectomy and illustrating his results. Not intended as a reference book or careful description of technique, this monograph informally discusses some of the problems related to the surgical treatment of hypertension.

Mental Health and the Prevention of Neurosis. By Joachim Flescher, M.D., Assistant Clinical Director, Child Guidance Institute, Jewish Board of Guardians, New York. With preface by Nolan D. C. Lewis, M.D., Director, New York State Psychiatric Institute, New York. Cloth. \$5.95. Pp. 605. Liveright Publishing Corporation, 386 Fourth Ave., New York 16, 1951.

In this book the author considers the process of rational education of instinctual drives based on psychoanalytic concepts in an attempt to offer safeguards against the development of neurotic patterns of living. The innate limitations to any guarantee of the success of such an effort, as the author himself points out, are the limitations that may be imposed by psychological rejection of the child by the mother, both in her gestational and immediate postnatal nutritional relationship, and the specific realities of the external environment, which can be of such magnitude that even the most favorably developed psychic economy will be forced to surrender in part.

The book is divided into three parts, covering instincts and environment in childhood, normal psychoinstinctual development, and abnormal development and psychoinstinctual disorders. A chapter on the psychological advantages of parenthood is particularly interesting. Here the author points out the fact that parents themselves may derive direct benefit from children by intelligently observing and dealing with the problems of the child in his various stages of development. The parent, in a sense, is thus allowed to relive some of the pleasures and difficult problems of his own early childhood through identification with the children.

The author's purpose in presenting this book is to bring together all the accumulated information in psychology that may be effectively applied in practice by psychologists, educators, parents, physicians, clergy, and other groups who practice psychological counselling.

Tara's Healing. By Janice Holt Giles. Cloth. \$3. Pp. 253. Westminster Press, Witherspoon Building, Philadelphia 7, 1951.

Tara Cochrane, a physician, was subject to insomnia and excessive use of sedatives. In the psychiatric ward of a veterans' hospital, frustrated, confused, and unhappy, he met a sergeant who had served under him in the Engineer's Corps during the war, with whom he went home to the hills of Kentucky. The story tells of the unfolding of a personality that had been distorted and cramped by strong childhood influences. Living the simple life of the hills, Tara learned the broader meaning of love for his fellow men and the joy of unselfish service and gradually became stronger and surer as he became absorbed in the persons around him. Within the framework of an exciting tale, Mrs. Giles has woven human interest, a bit of psychology and psychiatry, a sociologic study of the backwoodsmen of Kentucky, and a discussion of the belief and behavior of the "White Caps." This is told through Jory Clark, a preacher in the Church of the Brethren of Christ, called "White Caps" because of the caps worn by the women. His constant and contagious demonstration of his belief in a positive and active life of love and service to his fellow men is the major influence in Tara's healing. This story is fast moving, exciting, and at times highly emotional. It also has a moral value, which is often missed in the confusions of modern civilization. It is well worth reading.

Twentieth Century Painting. By Hugo Munsterberg. Cloth. \$5. Pp. 102, with illustrations. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1951.

This book should be of interest to the large number of physicians who find relaxation and self-expression in painting and sculpture. This book deals with painting only, but the carry-over into the related media is obvious. After the introduction, the book deals with the impact of Picasso on the art of the twentieth century. Then Matisse is discussed and, after that, the subjects of abstract and nonobjective painting, expressionism, fantasy, and surrealism. The book is illustrated with 57 halftones and 1 color plate, showing the various styles of modern painting. The traditionalist will abhor it; the modernist will love it.

RHEUMATOID ARTHRITIS

TO THE EDITOR:—Three years ago, a woman, aged 49, had swelling and pain in her thumbs. After a few months, the fingers and wrists, and subsequently the ankles, feet, and knees became involved. Her history reveals a loss of weight of 15 lb. (6.8 kg.) during the past few years. She is always nervous, and the menses are regular. She is well developed and moderately well nourished but has obvious difficulty in walking. The wrists are of typically "seal flipper type," without apparent ankylosis. The patient was given cortisone from December, 1950, to June, 1951, by another physician, without improvement of symptoms. The dosage was apparently excessive, because moon face developed, and, with withdrawal of cortisone, moon face disappeared. Recently, a two weeks' course of corticotropin (ACTH) was given, with dosage as high as 80 mg. per day. This therapy lessened the swelling but did not lessen the pain; hence corticotropin was discontinued. It is my impression that the diagnosis is rheumatoid arthritis. I shall appreciate your suggestion as to therapy.

John W. Derbyshire, M.D., Sebastopol, Calif.

ANSWER.—This patient presumably has rheumatoid arthritis, in view of the symmetrical progressive polyarthritis of three years' duration; however, the diagnosis should be carefully reviewed. Roentgenograms should be taken of representative joints and of the chest, along with laboratory studies of the blood and urine and a complete general physical examination. Disseminated lupus erythematosus without skin manifestations is still a possibility and should be kept in mind. If it is assumed that the patient has rheumatoid arthritis, her failure to respond to cortisone is most unusual, but a case has occasionally been observed in which there has been a failure of antirheumatic effect in the usually recommended dosage, even with evidence of hyperadrenalism. The failure of the patient to be helped by corticotropin in the dosage employed is also unusual, especially since subjective improvement almost invariably precedes objective changes such as decreased swelling. It is possible that this patient's adrenal cortex was unresponsive or that her tissues have a marked potentiality toward the destruction of corticotropin at the site of injection. The absence of response is more probably due to either or both of two conditions: arthritis of marked severity or emotional factors that interfere with the control of symptoms by the usual forms of therapy. A period of careful conservative therapy should be instituted, consisting in complete or nearly complete bed rest, aspirin in regular dosage to tolerance, a diet more than adequate in protein and vitamins, and heat and active exercises for the involved joints. At the same time, a search should be made for disturbing emotional factors, and simple psychotherapeutic measures should be employed. Cortisone or corticotropin should be dispensed with during the period of conservative therapy, which should last at least six months. At the end of this time, the desirability of employing cortisone in sufficient dosage on a long-term maintenance basis can be evaluated.

YEAST CELLS IN FECES

TO THE EDITOR:—I have had two patients with a large number of yeast cells in their stools. Is there any treatment for an excessive amount of fermentation in the lower bowel?

Louis M. Pavellich, M.D., Raton, N. Mex.

ANSWER.—The presence of yeast forms in the stools is considered normal; however, yeasts are known to appear in excessive quantities in the stools of patients who have received antibiotics in quantities sufficient to depress the normal colonic

flora and, occasionally, as a primary condition. Instances of systemic moniliasis are associated with the presence of an excessive amount of yeast in all the body secretions. When yeast is present in excessive quantities in the stool, a chest roentgenogram and a sputum examination should be made to rule out the possibility of systemic disease. The treatment of moniliasis requires desensitization to the yeast found in the stool before any active therapy can be undertaken. This desensitization is accomplished by the use of a vaccine made from the recovered yeast cells. After desensitization, large doses of iodides, thiamine hydrochloride, and vitamin B₁₂ have been recommended. (Whitcomb, Milzer, and Kunstader: *J. Pediat.* 35:715 [Dec.] 1949). Yeast forms in the stool are easily confused with other encysted forms of intestinal parasites, and careful identification by a trained parasitologist may be required to differentiate the two. It should also be emphasized that "excessive fermentation" may not be related to the presence of yeast in the colon and that a complete study of gastrointestinal function and colonic flora should be made.

DAMAGE TO A SURGEON'S FINGERNAILS

TO THE EDITOR:—A 46-year-old surgeon who engaged in orthopedic work in the Army using much plaster of paris and doing much fluoroscopy prior to that, notices changes in his fingernails chiefly involving the left hand. There is a longitudinal splitting, together with bluish gray longitudinal striations starting as red streaks at the base of the fingernails, which are growing very slowly. There is also a small hyperkeratosis at the dorsum of the right middle finger. This condition was diagnosed as x-ray or plaster of paris damage. Treatment with vitamin ointments and vitamin B₁₂ medication, as well as avoidance of all irritating soaps, has had no effect. The blood picture is normal. Are there artificial nails available to cover the damaged nails?

Ernest H. Bettmann, M.D., White Plains, N. Y.

ANSWER.—The condition of the surgeon's nails might well be the effect of roentgen rays on the nails. There is a remote possibility, too, of fungus infection of the nails, although such a possibility seems unlikely from the description. It is questionable whether plaster of paris would produce such permanent nail changes. There is no specific treatment for nail changes following exposure to x-rays, other than massage of the base of the nail with a mild lubricant, and this accomplishes very little. The keratoses, however, should be observed closely and, in all probability, destroyed, as they are prone to become malignant over the years. It does not seem that the artificial nails worn by women would be practical or necessary in this situation.

COMPLICATIONS OF RHEUMATIC HEART DISEASE

TO THE EDITOR:—Would coronary artery embolism or ball valve thrombus of the left atrium be the most likely cause of sudden death in a patient with rheumatic heart disease, mitral stenosis, long-standing auricular fibrillation, and recent congestive heart failure?

M.D., New York.

ANSWER.—Both embolism of a coronary artery and occlusion of the mitral ostium by a large ball thrombus, leading to sudden death, are relatively rare events in the course of rheumatic heart disease. In a recent study at the Massachusetts General Hospital on systemic arterial embolism in rheumatic heart disease (*Am. Heart J.* 42:566 [Oct.] 1951), covering a period of more than 10 years and including 194 cases, with 39 autopsies, there was no instance of embolic coronary occlusion and only one case of fatal occlusion of the mitral valve by a large valve-like thrombus. Coronary embolism, however, is not too rare in the presence of superimposed subacute bacterial endocarditis, whereas sterile emboli of larger size, originating in the fibrillating left auricle, apparently tend to avoid small right angle branches of the aorta.

INTERFERENCE WITH TELEVISION SETS BY DIATHERMY UNITS

TO THE EDITOR:—I installed a new Federal Communications Commission approved diathermy unit, and it produced as much as or more television interference than my old unit. The same thing was true when a unit manufactured by another firm was tried. Has any satisfactory means of eliminating the interference been devised? Other than "Raytheon," do you know of any diathermy sets that do not cause television interference? Frank L. Perry, M.D., Woodstown, N. J.

ANSWER.—The F. C. C. has assigned the following bands within which medical diathermy and industrial heating devices must operate: 13,560 kilocycles plus or minus 6.78 kilocycles; 27,120 kilocycles plus or minus 160 kilocycles; 40,680 kilocycles plus or minus 20 kilocycles; and 2,450 megacycles.

Some television manufacturers picked an intermediate frequency, in the neighborhood of 27,120 kilocycles, for use in one of the stages of the television machine. Since this intermediate frequency and one of the frequencies assigned for medical diathermy are so close, it is possible for medical diathermy devices to interfere with these television sets. It is desirable that television manufacturers use some other frequency in an intermediate stage, which is not near those assigned for use of medical diathermy by the F. C. C. If such is the situation in your case, the trouble lies with the characteristics of the television receiver.

It is realized the physician still does not wish to interfere with his neighbor's television, even though he may be within his rights when using an F. C. C. approved type of diathermy device. An alternate suggestion would be to shield the room in which the diathermy machine is operated or to apply a filter to the television receiver.

TREATMENT OF LYMPHOSARCOMA—COLEY'S FLUID

TO THE EDITOR:—In a man, aged 70, generalized lymphosarcoma (proved by biopsy) involving inguinal, axillary, and posterior cervical lymph nodes has developed in the last six months. He has had 20 deep therapy x-ray treatments by a competent roentgenologist. His general condition up to now is satisfactory. Are there any new developments in therapy? What is the present opinion about the use of Coley's fluid?

James H. Cummings, M.D., St. Louis, Mo.

ANSWER.—X-ray therapy remains the primary and most effective method for treating lymphosarcoma. This agent should be employed as long as the patient continues to respond satisfactorily. Nitrogen mustard has occasionally benefited a patient temporarily and should be reserved for the widely disseminated form of the disease that cannot be adequately controlled by x-ray therapy. More recently, triethylene melamine, an agent closely allied to nitrogen mustard in its pharmacological action, has become available. Its chief advantage over nitrogen mustard is that it can be administered orally. Also, in far-advanced cases, corticotropin or cortisone has produced some lymph node regression and temporary improvement. Coley's fluid has fallen into disuse, and there appears to be no reason to believe that it would be effective in the treatment of lymphosarcoma.

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MULTIPLE LIPOMAS

TO THE EDITOR:—A patient has multiple lipomas that develop continuously. They vary from the size of a marble to the size of a fist. What is the etiology, and what can be done to prevent these tumors from reappearing?

E. N. Ascherman, M.D., Chicago.

ANSWER.—The cause of either lipomas or lipomatosis is not known. It is possible that this disease has some slight association with Von Recklinghausen's syndrome. Nothing is known that will prevent these tumors from reappearing. It is usually wiser to remove the larger tumors, as they have been known to undergo malignant degeneration.

SEQUELAE OF HYDROCYANIC ACID POISONING

TO THE EDITOR:—A family was accidentally exposed to hydrocyanic acid gas in the course of a building fumigation. All were given some sort of first aid, and at least one was unconscious for an hour or so. What, if any, residual effects might result?

M.D., Maine.

ANSWER.—Concerning the residual toxicity from acute hydrocyanic acid poisoning, it is the consensus of toxicologists that this poison can be chronically toxic and may cause neurological symptoms after a single subfatal exposure. The symptoms that accrue are cachexia, headache, dizziness, pallor, anorexia, dyspnea, and, especially, peripheral neuritis and lassitude.

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TREATMENT OF NARCOTIC WITHDRAWAL SYMPTOMS

TO THE EDITOR:—Has corticotropin (ACTH) ever been used to treat withdrawal symptoms of narcotic addiction? Would you outline the best method for withdrawal of methadone?

Lyddone Miller, M.D., Amherst, Va.

ANSWER.—Experiments at the National Institute of Mental Health Addiction Research Center, United States Public Health Service Hospital, Lexington, Ky. have shown that neither corticotropin nor cortisone is of any value in alleviating symptoms of abstinence from opiates. The question concerning withdrawal of methadone is not specific. It is unknown whether withdrawal of methadone from persons addicted to that drug alone is meant or whether withdrawal of methadone following substitution for morphine is in question. In the first case, all that is required is simple reduction of the methadone. Under proper institutional conditions, withdrawal can be accomplished in 7 to 14 days. In the second case, one should first ascertain the least amount of morphine that will prevent the appearance of withdrawal symptoms. This is termed the stabilization dosage and can usually be determined in two or three days. Once the stabilization dosage is known, 1 mg. of methadone can be substituted for every 3 or 4 mg. of the patient's accustomed dose of morphine.

As methadone is a cumulative, slow-acting drug, the patient should be given one-half his accustomed dose of morphine and one-half his calculated dose of methadone during the first day of substitution. During the second day, only methadone is given. After substitution of methadone has been effected, the calculated dosage should be maintained for two or three days. The total dosage can be adjusted upward or downward, depending on the patient's response. Thereafter, methadone should be withdrawn over the course of 7 to 14 days, depending on the patient's response. While withdrawal symptoms should be expected near the end of treatment, severe manifestations of abstinence are never seen when this particular type of withdrawal is used.

ELECTROCARDIOGRAPHIC CHANGES IN JAUNDICE

TO THE EDITOR:—What are the electrocardiographic changes in patients with jaundice? Are these changes due to a virus myocarditis, or are the same changes also seen in obstructive jaundice?

I. Lutfi Vural, M.D., Ankara, Turkey.

ANSWER.—Electrocardiographic changes can be observed in any type of hepatic icterus. However, the only alteration that can be ascribed to the cholemia is sinus bradycardia. Abnormalities of the S-T segment, of the contour of the T wave, and/or the Q-T duration, observed not infrequently in the course of icterus gravis or in hepatic coma, are usually due to the disturbance of the electrolyte balance associated with the latter conditions. In the case of acute infectious hepatitis, similar changes may sometimes be seen and may represent the electrocardiographic manifestations of a concomitant interstitial myocarditis.

HEALING OF "THIN" BONES

TO THE EDITOR:—*Why do thin, small persons have difficulty in forming new bone when fractures of the mandible occur? In place of a bony union, a fibrous union and, often, no union at all is obtained. 1. Does thin bone affect new bone formation? Do a weak and improper blood supply and thin, small canaliculi affect formation? 2. Is calcium metabolism affected in this type of person? 3. Is there a hormonal disturbance, due to some nervous reaction in these sometimes highly neurotic persons? 4. Do the sympathetic nervous system and psychotic factors play an important part in these fibrous unions and nonunions of bone?*

William H. Hyde, M.D., Brooklyn, N. Y.

ANSWER.—This questioner assumes certain facts, which may not universally be acceptable. The mandible has excellent bone healing powers after fracture, but union in it may be influenced by an improper period of, and inefficient efforts at, immobilization; the presence of infection admitted at the time of fracture, i. e., open fracture; and the small medullary cavity of the bone and a relatively small amount of cancellous bone compared to hard cortical bone, which is less vascular. Bony healing depends mainly on blood supply, and bone grafts or other splints may be required to establish immobilization or to enhance local blood supply to which the healing effort responds with good result. To answer the specific questions:

1. "Thin" bone is ambiguous in meaning. If demineralized bone is meant (principally lack of calcium salts, as shown in roentgenograms) this may be caused by age, hormonal influences, or lack of dentition—as in the old, edentulous jaw. Such bone may be found in persons, both men and women, at the menopause and after loss of teeth. If thin bone is to be interpreted as small or narrow bone, this may be a personal or familial characteristic and may include all the skeleton. It may be an expression of osteogenesis imperfecta or some other dyscrasia of bone. Such bones have a lessened blood supply and lowered osteogenetic power compared to normal bone. This is inherent in the type of skeletal structure, and the bones have smaller canaliculi and smaller blood vessels.

2. Calcium metabolism in persons with small or thin bones is not abnormal. The blood serum calcium can be determined; if it is over 11 mg. per 100 cc., osteitis fibrosa cystica generalisata may be suspected, and it can be investigated by other symptoms and laboratory findings. Careful study of the jaw roentgenogram is indicated. If blood calcium is normal, it is difficult to increase it by giving calcium, except in large amounts. It is doubtful that calcium metabolism enters into this problem.

3. There may be hormonal disturbances dating back to childhood, starting with a thyroid disturbance, and there also may be nutritional defects in adolescence. If "thin bone" appears in an adult, it may represent demineralization influenced by hormone defects, as from ovary or testis.

4. It has never been shown that the sympathetic nervous system or psychotic factors play an important part in fibrous union or nonunion of bone. Fractures occurring among inmates of insane asylums heal as well as those of other persons. Overly nervous or psychotic persons may not tolerate or yield to orthodox methods of immobilization, so that nonunion results. Assuming immobilization of the fracture has been complete and of sufficient length, local irritations by aseptic drilling of the bone followed by more immobilization is indicated, or an onlay bone graft may be used.

FREAK DIETS

TO THE EDITOR:—*The September issue of Holiday described a meat and high-fat diet not only for reducing but for vigorous health. This is contrary to what is advocated for the prevention of atherosclerosis. Please comment.*

A. I. Love, M.D., Chicago.

ANSWER.—Freak diets often do harm. A high-fat diet or a high-meat diet should not be prescribed for accomplishing reduction in weight. For reduction of weight, a patient needs a reasonably well-balanced diet in which it may be necessary rigidly to curtail the fats and the carbohydrates. The maintenance of

vigorous health also requires a balanced diet, preferably without undue emphasis on any one foodstuff. The ultimate cause of atherosclerosis is still under discussion, notably the part that cholesterol or related lipid-protein combinations may play. The proposed high-fat diet will probably add unduly to the patient's weight and thus, in addition to the other harmful effects of obesity, increase the hazard of atherosclerosis.

CONTACT DERMATITIS AND SHOES

TO THE EDITOR:—*A patient has had a recurrent dermatitis on the dorsa of both feet, which follows the outline of the tops of her shoes. I believe the dermatitis is due to the chrome used in the leather dye. The dermatitis heals when she wears nonleather shoes. Do you have information concerning shoe manufacturers who do not use chrome in dyeing leather?*

Winston C. Holman, M.D., Shreveport, La.

ANSWER.—It is not sufficient to assume that the dermatitis is due to chrome. It may be due to one of the other materials of the shoe, such as cement, glue, felt, canvas, polish, trimmings, or lining materials. Sometimes a change to shoes made by another manufacturer is sufficient to overcome the trouble. If that does not solve the problem, an effort should be made by means of patch tests to determine the irritating agent. For unusual cases such as this, manufacturers ordinarily cooperate willingly by furnishing samples of the various ingredients for the patch tests. A new pair of shoes can then be made, using a substitute for the irritating substance.

TREATMENT OF ACUTE LARYNGOTRACHEOBRONCHITIS

TO THE EDITOR:—*I am interested in the management of both the early stages of acute laryngotracheobronchitis and the later stages, after respiratory obstruction is marked. Should chemotherapy be withheld until there is a full clinical picture, or should treatment be started early, when the obstructive phenomena are anticipated?*

Herman Miller, M.D., Pennsylvania.

ANSWER.—As a general rule, if a child has general symptoms of an acute infection, a croupy cough, and a pharynx negative for *Corynebacterium diphtheriae*, a direct diagnostic laryngoscopy should be made, and swab specimens for diagnosis and sensitivity tests should be taken directly from the larynx. If facilities for this are not available, antibiotics should be given without delay, on the basis of the pharyngeal reports. Until now, our best results have been obtained with penicillin and streptomycin, but, if sensitivity tests are unfavorable for these drugs, chloramphenicol (chloromycetin®) may be used. The margin between safety and toxicity is too narrow to use the sulfonamides in children; moreover, their toxic symptoms (fever, cyanosis, hemolysis, depression, and anemia) are almost identical with the symptoms of acute laryngotracheobronchitis.

HISTAMINE IN HEADACHE

TO THE EDITOR:—*In THE JOURNAL (46:979 [July 7] 1951), there is a reply to a query regarding histamine in headache. The last sentence reads "The contraindications for histamine injections are cardiovascular disease, peptic ulcer and some types of allergy." It appears that some of the most recent work with histamine is not sufficiently well known to have come to the attention of the physician who answered the query. May I therefore refer your readers to the following works by Benjamin Bernstein: (1) Histamine in the Treatment of Peptic Ulcer (Rev. Gastroenterol. 14:129, 1947). (2) Acidity: Is It Related to the Ulcer Syndrome?, paper read at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 13, 1951. A relevant abstract of an article from Gastroenterologia, Basel, by Biro and Nagy appears in THE JOURNAL (46:969 [July 7] 1951).*

Not only is histamine not contraindicated in the presence of ulcer, but it appears that it will find an important place in the management of gastric and duodenal ulcer, regardless of the effect on gastric acidity.

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ADVANCES IN DIAGNOSIS AND TREATMENT OF SURGICAL PULMONARY DISEASE

James W. Nixon, M.D.

and

John F. Perry Jr., M.D., San Antonio, Texas

Although the majority of thoracic diseases that are potentially surgical come within the scope of the thoracic surgeon, it is evident to all practitioners that lesions of the chest that are amenable to surgical therapy must be recognized early. Obviously, proper care of the patient with chest disease cannot be carried out otherwise. Since the limit of this paper does not permit discussion of the diagnosis and treatment of chest disease in detail, consideration will be given only to some of the more recent advances in management of those lesions of the lung, pleura, and tracheobronchial tree that are frequently encountered by the surgeon and are of particular interest to the medical profession as a whole.

CARCINOMA OF LUNG

Diagnostic methods for the detection of carcinoma of the lung have been perfected to such a degree that one can expect a positive diagnosis in approximately 85% of the cases. The history of cough, pain, and hemoptysis should demand that first consideration be given to carcinoma in the differential diagnosis of mass lesions of the lung. One must not wait for weight loss, lassitude, and other manifestations of inoperable carcinoma. Radiological study of the chest by the usually accepted techniques will demonstrate in most instances an atelectasis, the result of bronchial obstruction due to an endobronchial lesion, an obstructive emphysema, or the existence of a solitary mass. By means of angiocardigraphy, Keil and Schissel¹ have developed a technique of differentiation between unresolved pneumonia and bronchogenic carcinoma. Their procedure may prove useful also in visualizing the vascular structures of the mediastinum as

well as detecting hilar lymph node enlargement due to metastasis. Vascular stenosis indicative of the encroachment of malignant tissue may also be revealed. Changes in the peripheral vascular pattern may serve to indicate the presence of a peripheral tumor or other lesion.²

Fifty per cent of the cases of pulmonary carcinoma can be diagnosed bronchoscopically.³ In addition to the direct visualization of the lesion, biopsy can be done. Bronchoscopy is again of value in the visualization of the vocal cords for mobility, of the carina for infiltration, of the major bronchi for possible displacement, and of bronchi or trachea for compression by extraneous lesions.⁴ These secondary changes may indicate to the bronchoscopist the presence of an extrabronchial mass or of an infiltrating one. Any carcinoma, easily diagnosed by direct observation through the bronchoscope, is probably incurable.

Cytological study of sputum and bronchial secretions may be expected to show an increase in the number of accurate preoperative diagnoses by at least 20%.⁵ Carabelli reports 82.4% to 92.5% correct diagnoses in pulmonary neoplasms through cytological study of endobronchially-obtained secretions.⁶ Some clinics report that an 85% incidence of positive diagnoses is obtained by use of Papanicolaou smears of bronchoscopically-obtained material and coughed-up sputum.⁷ In cases of accessible lesions, needle biopsy of the lung may permit positive diagnosis. This method has been challenged because of the danger of spread or of contamination or the production of a pneumothorax. However, Rosemond and co-workers³ report a series of 132 cases of needle biopsy without apparent complications. The operative

Read before the Section on Diseases of the Chest at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 13, 1951.

1. Keil, P. G., and Schissel, D. J.: The Differential Diagnosis of Unresolved Pneumonia and Bronchogenic Carcinoma by Pulmonary Angiography, *J. Thoracic Surg.* 20: 62 (July) 1950.

2. Steinberg, I.; Dotter, C. T., and Andrus, W. DeW.: Angiocardigraphy in Thoracic Surgery, *Surg., Gynec. & Obst.* 90: 45 (Jan.) 1950.

3. Rosemond, G. P.; Burnett, W. E., and Hall, J. H.: Diagnosis of Carcinoma of the Lung, *J. Internat. Coll. Surgeons* 14: 100 (July) 1950.

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mortality rates with pneumonectomy for carcinoma of the lung have now been reduced in most clinics to about 5%, which compares favorably with the operative mortality rate for carcinoma of the stomach. This low operative mortality should furnish adequate reason for emphasis now to be placed on early diagnosis, if there is to be any further improvement in survival rates following pneumonectomy for lung carcinoma.

Harrison,⁸ quoting Ochsner, reports that, of every three patients who are sent to a surgeon with carcinoma of the lung, one has an obviously inoperable lesion, in one the lesion proves nonresectable, and one has a resection. This report certainly proves that patients are reporting to their family physicians too late after the onset of chest symptoms and that physicians are spending too great a period of time in the diagnosis of such lesions. Shaw⁷ estimated that the average time elapsing between the appearance of symptoms and the first visit to a physician by such a patient is five months and that the average time spent in diagnosis of the disease is six months. It seems obvious, therefore, that many of these lesions become inoperable during this lengthy period. It is recommended that any mass lesion of the lung that cannot be definitely diagnosed during two or three weeks of observation should be examined by exploratory thoracotomy with direct biopsy if necessary.

Pneumonectomy has generally been accepted as the type of operation indicated in dealing with pulmonary carcinoma. However, lobectomy seems to have an advantage when uncertainty of diagnosis exists and in those instances in which pulmonary and cardiac reserve has been diminished, provided, of course, that the lesion in question can be excised by this method. This less drastic operation would seem indicated also for small peripheral lesions that have no lymph node extension and for more

extensive lesions in cases in which only palliation can be achieved by excising the bulk of the tumor.⁹ Effler, quoting Adams, reports that in carefully selected cases the results following a lobectomy compare favorably with those following a pneumonectomy.¹⁰ Indeed, Churchill⁹ reports a 19% five-year survival rate following lobectomy as compared with a 12% survival rate following pneumonectomy. The importance of placing emphasis on diagnostic and therapeutic measures for the management of carcinoma of the lung is evident when one realizes that this disease comprises 7% of all cases of carcinoma seen at autopsy.¹¹

TUBERCULOSIS

Recently Katz and Lifschultz¹² described a method of bone marrow study for the diagnosis of acute hematogenous tuberculosis of pulmonary and extrapulmonary variety. Tubercle bacilli were found by smear and culture in 84% of a series of 78 cases. This method may prove to be valuable in the diagnosis of pulmonary tuberculosis of the hematogenous variety before obvious organ localization occurs. It is being used extensively with satisfactory results at the Brooke General Army Hospital by John G. Knauer.¹³

Surgical treatment of pulmonary tuberculosis can be divided into three categories: (a) collapse therapy, (b) drainage of cavities, either open or closed; and (c) pulmonary resections. Many authors¹⁴ agree that there is a definite place for pulmonary resection in the treatment of pulmonary tuberculosis but that our present limited experience with these procedures does not warrant our abandoning recognized and proved methods of surgical collapse; however, the indications for pulmonary resection are fairly well agreed upon. They are as follows: (1) thoracoplasty failure, (2) bronchostenosis and associated bronchiectasis, (3) tuberculoma, (4) lower lobe disease, (5) upper lobe disease unsuited for thoracoplasty, and (6) questionable diagnosis.

Lobectomy and segmental resection are to be preferred to pneumonectomy except in cases in which such extensive disease exists that the problem cannot be dealt with by more limited procedures. Gebauer,¹⁵ in several cases, has used with good results wire-enforced dermal grafts for the correction of healed tuberculous bronchostenosis. Experience with this operation is, of course, limited, and surgical extirpation seems at the present time to be the more warranted procedure. Segmental resection of involved areas and lobectomy in cases in which the main lobe bronchus is involved have both been successful in dealing with tuberculous bronchostenosis.

As indicated by its designation, segmental resection is a procedure wherein only the bronchovascular components that combine to form a lobe are removed.¹⁴ It is of value in those cases in which the disease is limited to one or two anatomical segments of the lobe. The advantage of segmental resection lies in the minimal sacrifice of pulmonary tissue necessary to the success of the operation. Segmental resection is equally applicable to those other indications for pulmonary surgery when the criteria of segmental limitation can be fulfilled.

The solitary circumscribed shadow of the tuberculoma is readily confused with the peripheral type of pul-

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9. Churchill, E. D.; Sweet, R. H.; Souther, L., and Scannell, J. G.: The Surgical Management of Carcinoma of the Lung; Study of Cases Treated at Massachusetts General Hospital from 1930 to 1950, *J. Thoracic Surg.* 20: 349 (Sept.) 1950.

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14. (a) Brontigan, O. C., and Rigdon, H. L.: Resection of the Lung in the Treatment of Pulmonary Tuberculosis, *Ann. Surg.* 60: 520 (March) 1950. (b) Day, J. C., and others: Resection in the Treatment of Pulmonary Tuberculosis, *J. Thoracic Surg.* 20: 854 (Dec.) 1950. (c) Chamberlain, J. M., and Klopstock, R.: Further Experiences with Segmental Resection in Tuberculosis, *ibid.* 20: 843 (Dec.) 1950. (d) Himmelstein, A.; Berry, F. B., and Read, C. T.: Lobectomy and Pneumonectomy in the Treatment of Pulmonary Tuberculosis; 10 Year Survey, *ibid.* 20: 866 (Dec.) 1950. (e) Jones, J. C., and Robinson, J. L.: Pulmonary Resection in Tuberculosis; Its Hazards, Indications, and Results, *ibid.* 20: 882 (Dec.) 1950. (f) Munz, C. W., and Adelman, A.: Pulmonary Resection for Tuberculosis with Streptomycin, *ibid.* 20: 892 (Dec.) 1950. (g) Sweet, R. H.: Lobectomy and Pneumonectomy in the Treatment of Pulmonary Tuberculosis; Subsequent Report, *ibid.* 19: 298 (Feb.) 1950. (h) Hughes, F. A., and others: Pulmonary Resection and Streptomycin in the Treatment of Pulmonary Tuberculosis, *Dis. Chest* 18: 244 (Sept.) 1950. (i) Chamberlain, J. M., and Ryan, T. C.: Segmental Resection in Pulmonary Disease, *J. Thoracic Surg.* 19: 199 (Feb.) 1950.

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16. Culver, G. J.; Concannon, J. P., and McManus, J. E.: Pulmonary Tuberculomas; Pathogenesis, Diagnosis, and Management, *J. Thoracic Surg.* 20: 798 (Nov.) 1950.

monary carcinoma. Culver and co-workers¹⁶ have differentiated tuberculomas into a surgical and a non-surgical group on the basis of calcification. We feel that any peripheral lesion that is not well calcified or proved to be nonmalignant should be resected segmentally, if possible, or dealt with by lobectomy or pneumonectomy.

Tuberculous lesions of the lower lobe form a group particularly suitable for resection because the anatomic location of the lesion makes them unsuited for thoracoplasty. Certain upper lobe lesions that may prove to be more suitable for resection than for thoracoplasty include (a) tension cavities, (b) scattered nodular infiltrates with fibrosis and with indistinct areas of rarefaction, suggesting small cavities, which are usually firm and inelastic, (c) lesions so situated in the lobe as to require an extensive thoracoplasty with needless sacrifice of pulmonary tissue, (d) some giant cavities, especially those in the gutter, and (e) progressive caseous pneumonic disease limited to an upper lobe, occurring in children or young adults.¹⁷ Further experience with primary resection of upper lobe lesions is necessary, however, to permit full evaluation of this procedure.

In cases in which a lesion is suspected but not proved tuberculous and in which there is the possibility of an existing carcinoma, the patient should be subjected to exploration of the chest.

Streptomycin¹⁷ is a proved valuable adjunct in surgery of pulmonary tuberculosis. The incidence of complications and of morbidity has been greatly reduced by its use, both preoperatively and postoperatively. As to the value of viomycin¹⁸ in the treatment of tuberculosis clinically, a final estimate cannot be made, since a more prolonged and a more definite clinical trial must be awaited. This drug has been shown to be active against mycobacteria, both in vitro and in vivo, and its toxicity in humans is apparently not very great. The manifestations of toxicity that do occur are renal irritation, abnormalities of serum electrolytes, elevation of blood urea nitrogen, and occasional impairment of vestibular function. Preliminary studies suggest that these are reversible changes.^{18c}

Segmental resection, lobectomy, and pneumonectomy have a definite place in the surgical treatment of pulmonary tuberculosis, provided one chooses his cases carefully and never forgets that he is removing only a major focus of a more widely disseminated disease.

ARTERIOVENOUS FISTULA

Arteriovenous fistula of the lung is a clinical entity that has been recognized for only a few years. Apparently this pulmonary lesion represents a manifestation of a more general telangiectatic tendency. Patients with this illness usually are thought first to be suffering from congenital heart disease, because of their polycythemia, digital clubbing, and cyanosis.¹⁹ Polycythemia vera may also be considered.²⁰ After the heart has been proved normal and after the x-ray has demonstrated a pulmonary lesion, the diagnosis of arteriovenous fistula of the lung should be made.

There is usually a loud murmur over the pulmonary lesion. Removal of the involved portion of the lung will result in immediate loss of cyanosis, a return of the blood cell count to normal, and a consequent cure of the patient.

CYSTS OF THE LUNG

Cysts of the lung may be either of two types, congenital or acquired. The latter type is the result of subpleural rupture of adjoining alveoli, forming blebs or bullae.²¹ The two types may be differentiated pathologically by the observation of lining epithelium and elements of lung tissue within the wall of the congenital cyst. Potts and Riker²² have described cystic-appearing areas in the lungs of infants with staphylococcic pneumonia. Cysts of either the congenital or the acquired type should be excised if symptoms are occurring because of the size of the lesion, the complication of infection or of hemorrhage, or because of a spontaneous pneumothorax. Pneumatoceles resulting from staphylococcic pneumonia apparently resolve spontaneously. Whether segmental resection, lobectomy, or pneumonectomy is indicated must be determined in each case.²³

CHRONIC EMPYEMA

Decortication²⁴ has been used in the treatment of tuberculous and mixed empyemas with some success; however, it is in the case of the neglected hemothorax that decortication operations have been most successful, and in these the best functional results have been obtained. Development of the technique of pleural decortication has given us a method whereby the chronic empyema can frequently be successfully dealt with. By means of this operation, the collapsed lung of chronic spontaneous pneumothorax can be re-expanded, provided that at the time of decortication the leak in the lung is simultaneously sutured.²⁵ Thoracic scoliosis resultant from chronic empyema can be corrected and frequently

17. Day and others.^{17b} Chamberlain and Klopstock.^{17c} Munz and Adelman.^{17d} Hughes and others.^{17h}

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prevented by decortication of the involved hemithorax and application of the proper orthopedic procedures subsequently to the spine.²⁶

CHRONIC SUPPURATIVE DISEASE OF LUNG

Employment of staged pulmonary resections offer patients with bilateral bronchiectasis a reasonable chance of recovery.²⁷ It has been found that the incidence of postsurgical complications is considerably lower in uncomplicated bronchiectasis than it is in the presence of superimposed acute suppurative disease. The incidence of bronchial fistula formation is greater with acute suppuration because of the inflammatory involvement of the hilum. This is a complication that makes for poor healing of the bronchial stump.²⁸ Lobectomy for one side, and later for the other, is the procedure of choice.

The improvement in prognosis of lung abscess is due to three factors: (a) the liberal use of blood, (b) the use of antibiotics, and (c) the change of surgical technique from drainage to excision of lung abscess.²⁹ Very small abscesses may be removed by segmental resection or may be shelled out of their capsules.³⁰ However, for abscesses over 3 cm. in diameter, it is better to employ lobectomy, because of the usual associated bronchiectasis in the lobe. The question has been raised³¹ as to whether segmental resection is an adequate extirpative procedure for chronic suppurative disease of the lung, such as bronchiectasis or abscess, since suppuration is usually manifest throughout the entire lobe. Segmental resection is adequate for small lung abscesses or for those involving the lingula, since actually the lingula represents a lobe anatomically. For larger abscesses, lobectomy is to be preferred.

Experience with the surgical repair of the trachea and bronchial tree has to date been limited to experimental extirpation and reconstruction of the trachea and bronchi,³² and to the clinical application of this work by Gebauer, who with wire-enforced dermal grafts has successfully repaired bronchi stenosed by tuberculous tracheobronchitis. He has obtained limited functional results in these cases. The long-term results of this work, however, must await the test of more time. The procedure of thoracobronchotomy³³ with approach to bronchial tumors through a transthoracic route and by opening the bronchus through its membranous portion is a merited one. By this technique the extent of endobronchial tumors extrabronchially can be fully determined and any indicated extirpative procedures then carried out.

Pulmonary coccidioidomycosis is now being successfully treated surgically.³⁴ However, as indicated in the surgical treatment of tuberculosis, one must bear in mind that coccidioidomycosis is a disseminated disease and that only a major focus of the disease is being removed. Apparently, surgical removal of a pulmonary focus of coccidioidomycosis does not cause spread of the disease. Indications for surgical removal of an involved portion of lung are as follows: (a) persistent cavities; (b) rupture of cavity with pneumothorax and empyema, (c) persistent hemoptysis, (d) coccidioma, (e) nonexpandable lung, and (f) failure of medical treatment.^{34b}

The alveolar cell tumor or pulmonary alveolar adenomatosis is a comparatively recently accepted entity. The

relationship of this lesion to the disease of sheep, known as jagziekte, is recognized though not fully understood. Jagziekte is apparently transmitted from affected to healthy animals. Pathologically, it resembles the human disease and is thought by some to be of viral origin, because of the apparently infectious character of the lesion. In man, the lesion appears to be of multicentric origin, manifested by respiratory symptoms of cough, dyspnea, and expectoration of moderate amounts of mucoid or foamy sputum. Diagnosis is positive only with thoracotomy and biopsy of the lung. The disease is progressive and fatal, and, even though the involved lung tissue is removed, recurrence will follow. Death usually occurs from respiratory failure before metastasis.³⁵ Although this disease has been recognized principally because of more frequent surgical exploration of the chest, it is apparent that surgical management is not the answer in dealing with the alveolar cell tumor.

SCALenus ANTICUS NODE BIOPSY

Mention should be made of a scalenus anticus node biopsy, a rather minor but important surgical procedure in the diagnosis of certain pulmonary diseases. Biopsy of lymph nodes over the lower end of the scalenus anticus muscles may reveal Boeck's sarcoid or carcinoma of the lung before either of these can be diagnosed by any other means.³⁶

SUMMARY

Some of the commoner surgical diseases of the lung are discussed. The present accepted methods of management of these lesions are explained.

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Changing Causes of Death in Childhood.—The so-called degenerative conditions—cardiovascular disease and cancer—now cause more deaths among children of school age in the United States than all the infectious and parasitic diseases combined. . . . Within recent years, the long-term trend of decreased mortality from infectious diseases has resulted in a change. . . . The infectious diseases are no longer more frequent than other diseases as a cause of death among school-age children. In 1948, cardiovascular disease and cancer deaths totaled 4,514 in the 5 to 19 age group, while the infectious and parasitic diseases accounted for 3,990 deaths in the same age group.—Harold A. Kahn, *Changing Causes of Death in Childhood*, *Public Health Reports*, Sept. 28, 1951.

RECENT TRENDS IN TREATMENT OF PULMONARY TUBERCULOSIS

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Among all the diseases to which human flesh is subjected tuberculosis still remains the first cause of death in the world. The death rate from this scourge has been markedly decreased in the United States, but the morbidity rate remains comparatively high. It might be well to remember, too, that there are places in the western hemisphere where the death rate is not 20 to 30 per 100,000, as it is in the United States, but 500 per 100,000. With modern rapid means of transportation and the consequent increase in mingling of peoples between countries, the control of tuberculosis poses an even greater problem from the epidemiological standpoint. To meet this increasing problem, and in an effort eventually to eradicate the disease, scientists and practitioners of medicine have for the past several years redoubled their efforts to find a biologic cure for tuberculosis. Any chronic disease for which there is no specific cure naturally has a multiplicity of treatments, which are used from time to time. It is well, therefore, to pause in our progress and try to evaluate the methods used in order to plot an even better and more accurate course toward final victory over our enemy—tuberculosis. Some of these methods may change in the next few months, so that much of what is written now may have to be revised before next year—just as some of what might have been written last year may be changed now. It behooves the general practitioner to keep abreast of developments in the treatment of tuberculosis and adapt the more appropriate ones to the care of his own patients. We shall now review the methods that are generally used today for the treatment of pulmonary tuberculosis, realizing that they are not to be considered the final word in the care of patients with this dread malady.

GENERAL CONSIDERATIONS

Once the diagnosis of pulmonary tuberculosis has been confirmed, assuming a reasonable degree of intelligence on the part of the patient, the first obligation facing the attending physician is to explain carefully to him some of the fundamental characteristics of his disease and advise him on a course of treatment in the light of what is known at that time about the patient's physical, emotional, and economic condition. The physician should begin to "condition" the patient for the journey ahead of him and proceed to lead him down the road to recovery.

In the treatment of pulmonary tuberculosis rest and diet are still the basic principles on which the physician builds and plans his campaign against the disease. The plan of medical care must also take into consideration the socioeconomic factors involved for these sometimes influence the methods to be used in applying the principles of therapy. Since there are many more patients to be treated than there are hospital beds in which to treat them, many will have to be cared for in their homes, and this circumstance may lead to modifications in the treatment regimen. This condition should not, however, be a

cause for withholding expert care from the home patient. With the exception of major surgical procedures, such care can be given, even though it causes the attending physician and the patient's family some inconvenience.

For those of us who have lived through several "sure cures" for tuberculosis, further new methods of therapy may be met with understandable skepticism. There are, however, measures that deserve serious attention and evaluation from time to time. At intervals since the time of Hippocrates attention has been given to diet in tuberculosis. Many special diets have been devised, with the view of giving the patient's tissues increased resistance against the tubercle bacillus and of improving his general nutrition. None have had any specific effect on the outcome of the disease. It may be mentioned in passing that while the use of extra proteins in the form of hydrolysates in preparing the patient for surgical intervention may be helpful, the routine use of such therapy has no real place in controlling the disease.¹ It is generally believed now that uncomplicated pulmonary tuberculosis requires only a well-balanced diet, including sufficient minerals and vitamins. Tonics may be employed occasionally in an attempt to stimulate appetite, but this is best accomplished by controlling the toxemia which accompanies the more acute stages of the disease.

For the patient at home in contact with his family, the control of symptoms may become a more important factor in his care.² For the fever and sweats uninterrupted rest and hydrotherapy are best. Proper care of the skin is important for patients who spend most of their time in bed. Many patients can be taught to control their cough, giving way to that reflex only when it is productive, thus reducing the use of cough sedatives, which often upset the stomach and cause loss of appetite and constipation. Hemoptysis from pulmonary tuberculosis in most cases stops of itself. The patient and family must be made to understand this, so the patient will not be unduly alarmed by the occurrence of this frightening and spectacular symptom. The treatment of hemoptysis is so universally understood that it need not be repeated here. We would only caution against the injudicious use of sedatives and morphine. One has only to see a patient cyanotic and gasping for breath as he drowns in his own blood to realize the danger of oversedation in these instances. The patient should be encouraged to clear the blood from his bronchi, since the threat of the spread of the disease is more serious than the danger from the loss of blood. Pain can be relieved by the application of heat to the

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chest wall or by the administration of analgesics. It is important to explain carefully to the patient some fundamental facts about the characteristics of his disease, so the symptoms will be better understood and he will cooperate better during the long period of his treatment. During the patient's initial period of bed rest, his progress should be watched carefully to help determine what further treatment may be required.

ANTIMICROBIAL THERAPY

Here enter the newer aids in the treatment of pulmonary tuberculosis. The wise practicing physician will select those definitive measures that so far have proved of most value and adapt them to use in individual cases. Unless one has adequate facilities for research, it is best to evaluate the results of professional research scientists and use those methods that seem best suited to the needs of one's individual patients. Antimicrobial agents have earned their place in present day therapy. Many such agents have been tried. Up to the present some have not given the favorable results hoped for. Among these are terramycin, aureomycin, neomycin, mycomycin, sulphathione³ (4,4'-bis[γ -phenyl-N-propylamino] diphenylsulfone-tetrasodium sulfonate),³ colloidal copper morphuate, glucosulfone sodium (promin⁴), thiazolsulfone (promizole⁵), and tibione (4-acetyl-amino-benzaldehyde-thiosemicarbasone).⁴ Refinement of some of these agents may make them more acceptable later. The use of streptomycin-paraaminosalicylate intramuscularly once daily for 90 days has shown some promise in a small number of patients, and it seems to delay the emergence of resistant strains of organisms.⁵ Further study will be required to confirm early results.

Streptomycin, dihydrostreptomycin and paraaminosalicylic acid are the chemotherapeutic agents of choice at the present time. When used judiciously they give more hope of controlling the disease and bringing an "arrest" than any other drugs we now have at our disposal. One must know their potentialities for harm as well as their power for good before risking their use.⁶ The choice of a chemotherapeutic agent and the time of its use present a problem in treatment of pulmonary tuberculosis. Particularly should one consider the toxicity of a drug, the possibility of emergence of resistant strains of organisms, and concomitant therapeutic measures to be used. Given in doses of 2 to 3 gm. daily, dihydro-

streptomycin is less toxic than streptomycin, and also less effective. In some series of cases a strain of germs resistant to dihydrostreptomycin developed in over 40%. In another series streptomycin given alone effected about 80% incidence of resistance at the end of 120 days of treatment.⁷

Streptomycin has been found the most effective single agent so far in treatment of tuberculosis.⁸ Its therapeutic effects are largely due to the suppression of the tuberculous infection, with prevention of new lesions, but without producing a biologic cure; nor does it give assurance against relapse. Results with this drug are largely dependent on the character of the disease—it works better in the acute phases and in mucous membrane tuberculosis.⁹ The drug does sometimes help in chronic tuberculosis, especially in conjunction with collapse therapy. The present trend is toward smaller doses given intermittently, that is, 1 gm. every other day or twice weekly.¹⁰ The administration of 10 to 12 gm. of paraaminosalicylic acid (PAS) by mouth daily, with intermittent injections of streptomycin, is rapidly gaining favor with phthisiotherapists. Given in this fashion, resistance is delayed, and the patient derives benefit from the drugs over a longer period of time.¹¹ This treatment regimen is particularly valuable in preparing a patient for major thoracic surgical intervention and should be continued through the time of the surgical procedures and for several months afterward. In this way many patients are enabled to receive the benefits of surgical intervention who otherwise would be very poor risks indeed. Combined intermittent streptomycin therapy gives encouraging results as viewed on the roentgenogram; the "conversion" rate of sputum is highest, and the toxicity is less. In general, the efficacy of antimicrobial therapy decreases with the chronicity of the disease and to a lesser degree with the extent of the disease. It seems unnecessary to warn that evidences of toxic manifestations should be watched for all during the course of streptomycin and for a short time afterward.

We believe that it is safe to advise against the routine use of streptomycin in minimal cases of tuberculosis. Most of the patients will recover with the more conventional regimen, and it is not wise to run the risk of developing in them a streptomycin resistant germ. Some very interesting work has been reported recently in which patients were given streptomycin intermittently and paraaminosalicylic acid daily for 12 to 17 months, and then the residuals of their disease were resected in an attempt to obtain a biologic cure. While the early results are rather striking, this method of treatment needs to be studied further before proper evaluation can be made. The method presents a different concept of the "cure" of tuberculosis.

COLLAPSE MEASURES

In addition to chemotherapy, or in conjunction with it, collapse therapy occupies an ever increasing place of importance in the care of the tuberculous patient. Collapse therapy may be used to provide local rest, to correct an unfavorable mechanical situation, such as the presence of a cavity, to accelerate the healing process, or to tailor the thoracic wall to fit the functioning lung. One of the older forms of collapse therapy is artificial pneumo-

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thorax. In the last few years the indications for its use have been rapidly constricted. In some hospitals now it is almost as hard to demonstrate artificial pneumothorax to medical students as it is to find a patient with typhoid fever or smallpox for their clinical instruction. We do not believe, at the present time at least, that this form of therapy should be abandoned entirely because in selected cases we still see good results from its use. Perhaps a part of its disfavor at present is due to its former misuse, as well as the development of other methods of collapse. Pneumothorax should not be attempted until the acute febrile reaction to the disease has subsided. To do otherwise invites complications that in themselves hinder the progress of recovery and may cause the abandonment of the treatment that was counted on to bring relief.

Pneumothorax finds its chief place in predominately unilateral lesions. Subapical cavities with surrounding pneumonitis often yield to this type of therapy. A lesion that fails to regress under sanatorium care, especially if the sputum remains positive, may improve when a successful pneumothorax is established. Where there is bilateral disease pneumothorax may be employed on the better side to prepare the patient for surgical intervention on the worse side. The hoped for results with pneumothorax are selective collapse of the diseased area and partial functioning of the normal portion of the lung.¹² This collapse is then maintained over a period of years, during much of which time the patient carries on his normal pursuits. As soon as the lesion is considered firmly healed, the lung is slowly reexpanded. The evaluation of the effectiveness of a pneumothorax must be made in the first few weeks following the initial puncture. Pleural adhesions present must be cut and an effective collapse established. If this cannot be accomplished, it is a wiser course to reexpand the lung early, thus avoiding what may be dangerous complications and sparing the patient expense and loss of time in starting a more effective form of treatment. For a pneumothorax to be considered successful, cavities must close and sputum must become negative. We consider the following as reasonable indications for the early reexpansion of a pneumothorax: (1) pleural adhesions that cannot be cut safely; (2) persistent pleural effusion; (3) cavities that persist or enlarge; (4) atelectasis of underlying pulmonary tissue; (5) recurring spontaneous collapse; (6) thoracoscopic discovery of subpleural tubercles.

Any one of the above conditions spells failure for the pneumothorax and may lead to one or more of the following complications: (1) empyema; (2) spontaneous pneumothorax; (3) unexpandable lung; (4) obliterative pleuritis; (5) air embolism. It is much wiser and a more courageous procedure to tell the patient frankly that the treatment is not accomplishing what was hoped for than to persist in carrying on an unsuccessful regimen that may endanger his chances of recovery. It is believed today that 75 to 80% of the patients with pulmonary tuberculosis will not be benefited by pneumothorax. These patients are the ones with (1) pleural symphysis; (2) tuberculous pneumonia; (3) tuberculous bronchitis with evidence of bronchial obstruction¹³; (4) extensive pulmonary destruction; (5) tension cavities; (6) tuberculoma or tuberculoma-like cavities; (7) acute pleurisy with effusion; (8) dyspnea due to emphysema or decom-

pensated cardiac disorders. These contraindications obviously severely limit the number of patients suitable for pneumothorax treatment.

PULMONARY RELAXATION

The value of diaphragmatic paralysis in the treatment of tuberculosis has been under discussion for many years. It seems fair to state that mere relaxation of the diaphragm could not be expected to yield a great influence on pulmonary lesions. Yet the addition of this therapy may be enough to allow a lesion to heal which would not heal without this aid. As a rule diaphragmatic paralysis should be temporary, since permanent loss of diaphragmatic function, with no assurance of healing the tuberculous lesion, is a gamble not worth taking. With proper understanding of the anatomy of the phrenic nerve, it can be interrupted in such a way that function should return in all but a very few cases within six to eight months. If it is advisable to continue the paralysis beyond that time, the operation can be repeated. Perhaps the most widely accepted indications today for diaphragmatic paralysis are: (1) as an adjunct to bed rest in early lesions; (2) in some patients with cavity when a more definitive collapse measure cannot be used; (3) in certain lower lobe lesions; (4) in conjunction with pneumothorax or pneumoperitoneum; (5) occasionally to help obliterate pleural space in the presence of empyema. There is some disagreement among the profession even on these indications.

The observation that air introduced into the peritoneal cavity accidentally had a beneficial effect on tuberculous lesions in the lungs has led to the use of artificial pneumoperitoneum as a primary procedure or as an adjunct to phrenic nerve surgery. In the last three to four years there has been in many places throughout the country a noticeable shift in treatment from pneumothorax to pneumoperitoneum. The indications for both are changing from month to month, but in all probability there will be a leveling off period soon. At the present time this procedure is indicated: (1) in minimal lesions, especially acute exudative ones, as an adjunct to bed rest; (2) in moderately advanced lesions with small or moderate-sized cavities when pneumothorax has failed; (3) in advanced bilateral cases too extensive for other collapse therapy; (4) to control exudative lesions prior to thoracoplasty; (5) in the old age group with complicating emphysema; (6) to help obliterate empyema cavity; (7) in basal lesions beneath upper thoracoplasty; (8) after resection.

This form of therapy is contraindicated in cases of heart failure, in moribund patients, during the latter months of pregnancy, in the presence of large abdominal tumors, or in the presence of uncontrolled hernias. The relaxation and elevation of the diaphragm afforded by the procedure may favorably influence the course of the disease so that a more definitive measure can be used later. Its use should be discontinued if significant ascites occurs, or if the patient finds it seriously interferes with eating. Serious complications with this therapy are rare, and it can be discontinued easily.

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SURGICAL TREATMENT

Surgical intervention in the treatment of pulmonary tuberculosis occupies a unique position in the field of surgery, in that it is not in itself definitive, but is merely an adjunct in the treatment of patients with this disease. Major surgical procedures used in the treatment of tuberculosis are of two general types: (1) those operations whose effect on the lung are direct, such as collapse therapy procedure, and (2) those operations performed on the lung itself, such as cavity drainage and resection. Formerly the patients referred to the thoracic surgeon for treatment were examples of failure of all other forms of therapy. This failure was due to late diagnosis, too little attention to the minimal lesion, and inadequate bed rest. There has been a tendency in the past to plan therapy according to a routine in which major surgical measures have been used only when other methods have been tried and failed. This concept does away with case selection and implies that the simpler procedures are harmless and in no way interfere with the success of major procedures. The old trial and error method is no longer justifiable.

The aim of all treatment of tuberculosis is the complete and permanent control of the disease and the return of the patient to a state of health consistent with comfort and a reasonable level of activity. Although surgical intervention is considered only an adjunct to treatment, it plays an increasingly important role in the management of patients with tuberculosis. Now tuberculous patients are considered for some type of collapse or surgical intervention, with the exception of those whose disease is so minimal that such treatment is not necessary or those whose disease is so far advanced that therapy of this type is impossible. Surgical intervention in tuberculosis is designed to augment the healing process through relaxation of diseased tissue by collapse, drainage, or actual resection of the major focus of the disease.

Relaxation may be all that is necessary to bring about complete healing, but chronic cavernous areas may need collapse. Cavity closure and resultant sputum conversion are the chief criteria of success in the treatment of pulmonary tuberculosis. One does not, however, overlook such important factors as the general nutrition of the patient and the eradication of all signs of activity of the disease.

Cavity closure may be influenced by many mechanical factors. Tuberculous tracheobronchitis is perhaps the most important factor operating within the lung which influences the closure of cavities. Obstruction of the bronchial lumen by ulcerating tissue and bronchial secretion may cause a valve-like action which places cavity areas under positive pressure. Such cavities resist closure, and unless this mechanical factor can be removed, it may be difficult to obtain a good result. The cavity wall may be so thick that closure will be impossible by collapse. In these tuberculoma-like cavities nothing but excision will suffice. The extent of the pericavernous involvement may influence the time taken to bring about cavity closure, so that one would have to wait a longer period for sputum conversion here than in patients hav-

ing cavities with thinner walls and less extensive involvement of adjacent tissue. The anatomic extent of the pulmonary lesion influences decisions regarding surgical intervention. The disease may be so minimal that surgical intervention would not have to be contemplated, or the extent of the disease may be so great as to render surgical intervention inadvisable, since there would be insufficient functioning pulmonary tissue to support life after the surgical program had been completed. Between these two extremes, however, there exists a group of patients who have disease of various extent who are suitable for surgical procedures that have been devised for the treatment of pulmonary tuberculosis. The general advance of the disease or deterioration in the condition of the patient may contraindicate or be cause for abandoning collapse therapy. The type of lesion, too, becomes an important factor in selection of cases for surgical intervention. The physiological as well as the chronological age of tuberculous patients must be considered. Thoracoplasty is a badly deforming operation on patients in the growth period and should not be used with these patients. Advanced age may not absolutely contraindicate certain of the major surgical procedures, but it might make them inadvisable in individual cases. The patient's immunologic response to the disease must be estimated. Pulmonary tuberculosis is a disease characterized by exacerbation and remission. The timing of the application of the various surgical procedures must be considered carefully in order to perform the operation at the time when the patient is in the best possible condition. Rest and chemotherapy are of great value in this regard. The patient's economic situation must also be considered. Some types of treatment must be continued over a period of months or years and entail considerable expense. Often the choice between two procedures, both of which offer a good chance of success, may be made purely on the economic basis. The temperament of the patient and his ability to cooperate may influence decision as to therapy. There are some people who are not temperamentally suited for an extensive period of treatment, which requires a great deal of self-discipline. In patients of this temperament a permanent type of collapse may be preferable.

Thoracoplasty has proved to be one of the most successful procedures in the surgical treatment of patients having pulmonary tuberculosis.¹⁴ The technique of this operation has been greatly refined so that the mortality is now less than 3%, and the good results that can be expected are in the neighborhood of 80 to 90%. This lowering of the mortality and increase in good results has been accomplished in spite of the fact that much poorer risk patients are now accepted for this procedure. Performing the operation in small stages instead of one large heroic surgical procedure has undoubtedly been the greatest contribution to the safety of this operation. A thoracoplasty should obtain adequate collapse and yet conserve as much pulmonary function as possible. Before a patient is accepted for thoracoplasty, he must be carefully evaluated from the standpoint of respiratory reserve to make sure he can tolerate the full program contemplated. It is an injustice to the patient to start a procedure if it stands very little chance of being completed.

14. Shaw, R. R.: Surgical Management of Tuberculosis, *S. Clin. North America* 24: 539, 1949.

Thoracoplasty is indicated in patients having cavernous disease in one lung in whom the other lung is free of disease, or the disease is at least quiescent. Thoracoplasty also may be useful to bring the disease gradually under control. It may be done with the realization that it probably will not bring about conversion of sputum. It may be undertaken with the frank realization that resection may be necessary as a later procedure. Thoracoplasty may be indicated to alter the chest wall in order to permit maximum use of the residual functioning pulmonary tissue in patients who have destroyed lungs or who have had resections. Absolute contraindications to thoracoplasty that are most generally accepted at present are: (1) extensive active disease in the contralateral lung; (2) inadequate respiratory reserve; (3) associated nonpulmonary disease of grave prognosis; (4) large solitary basal cavities; (5) tuberculoma and tuberculoma-like cavities; (6) tuberculous granulomas in the trachea and contralateral bronchi. Relative contraindications to thoracoplasty are: (1) minimal disease; (2) stenosis of a major bronchus; (3) bronchiectasis producing symptoms; (4) patient in growth period of life; (5) severe exudative tuberculosis; (6) advanced age; (7) cyst-like cavities which are probably epithelialized. This last group of contraindications are classified as "relative" because conditions conceivably can change so that they may no longer prove contraindications. While the results of thoracoplasty are improving from year to year, it must not be assumed that this operation is free from trouble. The following complications may occur: (1) spread of the disease; (2) atelectasis; (3) hemothorax due to tearing of the pleura; (4) wound infection; (5) inordinate postoperative pain; (6) loss of shoulder motion; (7) scoliosis; (8) dyspnea due to loss of respiratory reserve.

The extirpation of tuberculous lung tissue is not a new idea, but most of the knowledge and experience with this method of treatment have been gained in the last 10 years, during which time it has been used with increasing frequency. During the earlier part of this period, results were discouraging because of the relatively high operative mortality or the prohibitive incidence of serious complications. More recently, however, significant advances have been made in thoracic surgery and the fields of anesthesiology and bronchoscopy, so that the mortality and complications associated with lung resection have been markedly reduced. In fact, pulmonary resection can be performed today with such safety that it should be considered in any therapeutic program for the tuberculous patient. It should be stated that pulmonary resection is not a competing but a supplementary form of treatment to the established methods of rest and collapse therapy. In general, it can be used when simpler measures fail or cannot be expected to control the pulmonary lesion. It is difficult just now to present a categorical list of indications and contraindications for resection, but the most generally accepted indications today are: (1) bronchial stenosis sufficient to block drainage of the lung; (2) bronchiectasis complicating tuberculosis; (3) cavities in the lower lobes with the other lobes relatively clear; (4) tuberculomas or tuberculoma-like cavities; (5) epithelialized cavities; (6) post-thoracoplasty resection.

Where it can be employed, resection has some advantages over thoracoplasty—such as rapid conversion of sputum, fewer operative procedures, less deformity, and effectiveness where thoracoplasty would likely fail. It should be repeated though that resection does have the disadvantage at present of a higher mortality and a higher complication rate. One of the disadvantages of resection is that it forces other portions of the remaining lobes to overdistend to accommodate the remaining space. Many surgeons now attempt to overcome this disadvantage by performing a thoracoplasty on every patient who has had a lobectomy or pneumonectomy. It may be that this combination can supplant thoracoplasty as a procedure of choice in handling many patients with far-advanced tuberculosis. The two major complications of resection, pleural infection and spread or reactivation of disease, have been eliminated largely by careful technique, improved anesthesia, and the adjunct of antimicrobial therapy. It seems preferable at the present state of development to do a thoracoplasty instead of a resection in any patient in whom thoracoplasty conceivably can bring about good final results. This contention is supported by the experience that thoracoplasty patients in general do well and that the longer a series of thoracoplasties is followed the more good results will be found. In contradistinction to this, resection for tuberculosis seems to follow a line of diminishing returns, in that the longer any series of resections is followed the fewer good results are found.

Early surgical attempts to drain tuberculous cavities led to disastrous results. It was found that the opening of these cavities led to the introduction of secondary infection, so that the patient became much sicker and also had a painful draining wound. In an attempt to overcome the mechanical problem provided by blocked or tension cavities, Monaldi recommends drainage of such a cavity through the chest wall. Through a cannula a catheter is introduced directly into the cavity through the chest wall and is held in place after the cannula is withdrawn. Such drainage may reduce cough and toxemia and also improve the patient's general condition. Since the discontinuation of the suction often allows the cavity to reopen, the use of Monaldi drainage supplemented by thoracoplasty collapse is favored by many surgeons as a means of closing large tuberculous cavities. Cavity drainage by rib resection is a useful procedure in a very few patients who have had unsuccessful thoracoplasties or in whom thoracoplasty is contraindicated because of poor respiratory reserve or because of the position of a tuberculous cavity. As a rule these cavities must be drained by the use of a two stage technique to make sure there is proper pleural symphysis before the cavity is opened. Cavities are packed and treated in the same manner as a pulmonary abscess. The use of streptomycin mixed with plasma as a dusting powder will reduce the infection around the drainage site. This procedure is advocated as a means of salvaging a very small percentage of patients who cannot get well in any other way.

The necessity of performing thoracoplasty in several stages and the resulting deformity caused by thoracoplasty has led to a continuing search for an operation which will yield as good results without these disadvan-

tages. Various operations creating collapse by separating the parietal pleura from the endothoracic fascia have been devised. The maintenance of the space has been accomplished by the use of a variety of materials—i. e., air, oil, paraffin, fat, muscle, and plastic balls. Regardless of the space filling material used, all these operations have certain disadvantages compared with thoracoplasty. They are not safe over large cavities where the lateral wall of the cavity may be receiving some of its blood supply from the intercostal vessels. In these patients rupture of the cavity into the extrapleural space is not uncommon and results in a severe complication. Frequently a thick-walled cavity may be displaced downward by the extrapleural operation without closing it, which leaves an almost impossible therapeutic problem. Extrapleural operations have a limited number of indications in which maximum preservation of vital capacity is necessary in order to use another procedure to control disease in the opposite lung. While this treatment may be very useful to aid in arresting dis-

ease in a small group of patients with bilateral lesions, as a procedure by itself it certainly should not supplant thoracoplasty.

SUMMARY

In this paper attention is called to the fact that tuberculosis still presents a major health problem in the world today. There are certain basic fundamentals of treatment to be observed, the chief of which is rest. Great improvements in phthisiotherapy have been made in recent years through chemotherapy and collapse treatment. Surgical measures have brought to the field of tuberculosis therapy great aid and much encouragement in our struggle to eradicate this disease. Some of the indications and contraindications for measures in the present day treatment of tuberculosis are given, with the full realization that they may change from year to year as progress is made through further experience. The practicing physician is urged to study these measures, so that he may at all times adapt them to the best care of his patients.

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RECENT DRUG THERAPY IN DISEASES OF THE CHEST, INCLUDING TUBERCULOSIS

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At present, there are a number of effective drugs available for the treatment of many of the common acute pulmonary infections; for example, *Pneumococcus pneumoniae* can be controlled successfully by sulfadiazine, penicillin, aureomycin, chloramphenicol, or terramycin. It is desirable in many cases of pneumonia and in other types of pulmonary infection to determine the exact etiological agent and its sensitivity to the various antibiotics before beginning treatment. Unfortunately, this is frequently impossible because the patient's condition requires immediate therapy or laboratory facilities to perform the tests are lacking. Most hospitalized patients suffering from pneumonia now receive penicillin because of its low toxicity and low cost; however, in most cases, the advantage of oral administration is so great that any one of the three latter antibiotics are likely to become even more popular than they now are, if their cost is reduced. Since aureomycin, chloramphenicol, and terra-

mycin have a broad antibacterial spectrum, there is an additional advantage in their use, if the exact etiological diagnosis is uncertain. Penicillin is likely to be strikingly beneficial only in pneumonias caused by pneumococci and streptococci. Although staphylococcal pneumoniae are sometimes amenable to this treatment, they are often caused by penicillin resistant organisms. On the other hand, aureomycin, chloramphenicol, or terramycin control not only pneumococcal, staphylococcal, and streptococcal infections but also influenzal, coliform, tularemic and Friedlander's pneumonias. Pneumonias associated with Q fever, typhus fever, and spotted fever are also favorably influenced, as are primary atypical pneumonia and pneumonia associated with psittacosis and lymphogranuloma venereum.¹ Although the evaluation of antibiotic treatment of primary atypical pneumonia has been difficult because of its variable clinical course and generally good prognosis, controlled studies indicate that aureomycin is valuable in shortening the period of illness.²

Streptomycin should not be forgotten in the treatment of pneumonias. Its value in treating tularemic infection has been known for a number of years. It is effective in Friedlander's pneumonia³ and combined with sulfadiazine in treating influenzal infections.⁴ In an uncontrolled series of cases, it was reported effective in the treatment of primary atypical pneumonia.⁵ It has also proved to be the most valuable antibiotic in the treatment of plague.⁶

Lung abscess, acute, subacute, or chronic, is favorably influenced to some degree by antibiotic therapy. If properly handled, surgical intervention is unnecessary in most acute and many subacute abscesses. We found that a combination of parenteral and aerosol therapy was more effective than either used alone. As a rule, two in-

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jections of 300,000 units of procaine penicillin and four aerosol treatments were given daily. The aerosol solution was made up of 2 cc. of isotonic sodium chloride solution, 3 cc. of a chlorophyll derivative (chloresium®), and 500,000 units of crystalline penicillin. One cubic centimeter of the mixture was given at each treatment. Compressed air was used to avoid the danger of possible explosion, with air flowing at a rate of 4 to 6 liters per minute, and a racemic epinephrine solution (vapo-nefrin®) or a DeVilbiss no. 40 nebulizer. Chloresium® was principally useful in eliminating the bad odor of sputum, but perhaps had some antibacterial action as well. Therapy was continued until complete clearing of the pulmonary lesion, as seen in the roentgenogram, had taken place or until there was no further change in the residual shadows. The period of treatment was usually four to six weeks and sometimes longer. If the residual shadows were extensive and consisted of more than a few fibrous strands, resection of the involved portion of the lung was performed, not only for the purpose of removing infected and damaged residual pulmonary tissue but also because of the danger that a pulmonary neoplasm might be the basic cause of the lesion that resembled an abscess.

In most cases, acute exacerbations of the symptoms of bronchiectasis were relieved by short periods of treatment with combined parenteral and aerosol penicillin. Oral use of aureomycin, chloramphenicol, and terramycin also proved useful. However, at present, if feasible, excision of the involved portion of lung offers the best prospect of permanent cure. Antibiotics did not influence the condition of patients suffering from nonspecific pulmonary fibrosis, except with regard to the control of superimposed bacterial infections. In the management of the chronic suppurative bronchitis and bronchiectasis associated with cystic fibrosis of the pancreas, penicillin given parenterally and by aerosol, and particularly aureomycin, were found useful.⁷

Among the pulmonary diseases due to fungi, actinomycosis was treated successfully with large doses of penicillin, and with penicillin and sulfadiazine, the latter being more effective.⁸ A patient with severe, nonpulmonary actinomycosis recovered after aureomycin therapy.⁹ Among the three other relatively common fungus infections in the United States that involve the lung, there is no successful treatment for disseminated histoplasmosis and disseminated coccidiosis. In treating blastomycosis, iodide therapy, with prior desensitization to the fungus in patients having a positive intradermal test result, is the only available method of treatment with any promise of success at present.¹⁰

To date, no drugs have been found that have a proved, permanent influence on sarcoidosis or berylliosis, silicosis, or other pneumoconioses.

Much work has been and is being done in laboratories throughout the United States in an attempt to find additional and improved drugs for use in the treatment of tuberculosis. At present, streptomycin, dihydrostreptomycin, paraaminosalicylic acid (PAS), and amithiozone (TB-1) are used widely clinically, and neomycin, viomycin, and terramycin are being studied in widespread clinical investigations. Of the streptomycin and dihydrostrepto-

most effective. In the small doses now being given (1 gm. a day or less) one drug has little advantage over the other. They are equally effective therapeutically, and although the chief manifestations of toxicity of both involve the eighth nerve, streptomycin is more inclined to affect the vestibular branch and dihydrostreptomycin the auditory branch. The tendency of dihydrostreptomycin to cause deafness, particularly if given in large doses, was well substantiated in the case of the chloride salt of dihydrostreptomycin. That this is true of the sulfate salt of dihydrostreptomycin, which is now supplied by the drug companies, seems less likely but is still uncertain.

Paraaminosalicylic acid, when used alone in the treatment of tuberculosis, was found to be less effective therapeutically than streptomycin, but, nonetheless, of definite value. It is given orally, the usual dose being 12 gm. per day, in three or four divided doses. Toxic effects were limited to the gastrointestinal tract and consisted of dyspepsia, nausea, vomiting, and diarrhea. These were often absent and seldom severe, but, occasionally, patients were unable to tolerate the drug. Paraaminosalicylic acid is most effective when given in combination with streptomycin, emergence of tubercle bacilli resistant to streptomycin being thus greatly delayed.

Amithiozone was used extensively in Germany before being introduced into the United States. The recommended dose is 100 to 200 mg. daily, orally. Experience with amithiozone in the United States proved disappointing therapeutically. Toxic effects were common, particularly with doses of 200 mg. per day or more. There was, at times, nausea and vomiting, evidence of liver or kidney damage, anemia, and leukopenia. Any or all of these effects could occur in the same patient. When administration of the drug was stopped promptly, the toxic effects were found to be reversible in most patients. At present, amithiozone is usually reserved for the treatment of tuberculous patients who are in need of drug therapy and cannot tolerate streptomycin or paraaminosalicylic acid. Whether amithiozone, when given in combination with streptomycin, acts similarly to paraaminosalicylic acid in delaying the emergence of streptomycin resistant tubercle bacilli is still under investigation.

Neomycin, although active against the tubercle bacillus, in vitro and in vivo, has thus far proved too toxic for general use in the treatment of human tuberculosis. A high incidence of deafness and renal disturbance has occurred in the few patients treated.¹¹ Viomycin is highly active against the tubercle bacillus in the test tube and in the experimental animal.¹² The available data, which

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are admittedly small, indicate that it is somewhat effective in human beings. However, with regard to toxic effect, in addition to the effect on the vestibular and auditory nerves and kidneys, which is similar to that of streptomycin and dihydrostreptomycin, there were marked changes in serum electrolytes, consisting of hypokalemia, hypocalcemia, hypophosphatemia, and hypochloremia as well as an increase in carbon dioxide combining power.¹³ The mechanism of the effect on electrolytes is not understood. Although its peculiar toxic effect makes the management of cases difficult and a great strain is placed on the laboratory because of the multiplicity of tests needed for safety in long-term therapy, viomycin must be studied further to ascertain its place in the chemotherapy of tuberculosis.

The effect of terramycin on human pulmonary tuberculosis was disappointing; however, there is a possibility that it may have an effect similar to that of paraaminosalicylic acid in delaying the emergence of streptomycin resistant organisms. A study of this is under way.

At present, for patients whose tubercle bacilli are still sensitive to streptomycin, combined therapy with streptomycin and paraaminosalicylic acid is preferred. If streptomycin is given in doses of 1 gm. or 0.5 gm. daily or 1 gm. twice a week, with 12 gm. of paraaminosalicylic acid daily, almost identical therapeutic results are obtained. Perhaps the regimen employing 1 gm. of streptomycin twice a week, with 12 gm. of paraaminosalicylic acid daily, is best for most patients, since toxic effects are rare, and our present impression is that streptomycin resistant organisms are at least no more likely to develop than if streptomycin is given daily with paraaminosalicylic acid.

Although there have been occasional exceptions, most patients whose tubercle bacilli have become resistant to streptomycin have not shown such good results with further chemotherapy as those whose organisms remained sensitive. After combined treatment with streptomycin and paraaminosalicylic acid for four months there were streptomycin resistant organisms in only 15% of the patients whose sputum remained positive, whereas, if streptomycin was used alone, the sputum of about 80% of such patients contained resistant organisms. In many cases, this permitted longer periods of treatment with lasting beneficial results than was possible when streptomycin was used alone.

In addition to the ototoxic effect already mentioned in connection with both streptomycin and dihydrostreptomycin, evidence of renal toxicity, as shown by the presence of albumin, casts, and red and white blood cells in the urine, occurred in a small proportion of patients. This has become less frequent because of the lower doses used at present. In most patients, the presence of urinary abnormalities was of no consequence; however, in patients with renal failure, as evidenced by the presence of a high blood urea nitrogen and impaired renal function tests, streptomycin or dihydrostreptomycin should be used with great caution, if at all, since, in such cases, there was a strong tendency for the renal function to become worse.

Chemotherapy was found to be particularly useful in the treatment of patients suffering from acute advanced pulmonary tuberculosis. Its use, for example, in massive

tuberculous pneumonia completely altered the prognosis of this serious condition.¹⁴ In fact, it is now difficult to arrive at a prognosis before chemotherapy is tried, since many patients whose death seemed certain were saved, some temporarily, others living on with the disease in a chronic form, and a few even returning to good health. Most patients with very advanced disease should undergo prolonged treatment of at least eight months to a year. Chemotherapy was particularly beneficial in tuberculous tracheobronchitis. These lesions responded rapidly, and, usually, two to four months of treatment were sufficient. Contrary to earlier experience with streptomycin alone, we found that the so-called tension cavities responded well to a combination of streptomycin and paraaminosalicylic acid, particularly if treatment was prolonged for at least eight months. Unfortunately, chemotherapy was found to have much less value in the treatment of long-standing chronic pulmonary tuberculosis, and little more than the temporary relief of symptoms may be expected in such cases.

As an approximate summary of the study of the many regimens used by the Veterans Administration and army and navy hospitals, patients suffering from advanced, relatively acute pulmonary tuberculosis, after four months of treatment with streptomycin and paraaminosalicylic acid, may expect to find roentgenographic evidence of moderate to marked improvement in about 50% of the cases, slight improvement or no change in about 40%, and evidence of unfavorable progression in about 10%.¹⁵ After eight months of treatment, about 70% of the patients may be expected to show moderate or marked improvement.

In general, patients with minimal pulmonary tuberculosis should not undergo chemotherapy, because most of them derive as much benefit from ordinary methods of treatment. In any event, the importance of correlating chemotherapy with other methods of treatment cannot be stressed too greatly. Chemotherapy is not a substitute for prolonged bed rest, and the proper timing of the addition of collapse therapy, when appropriate, should be planned in each case on an individual basis, at the outset.

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Myocardial Infarction.—The growing tendency to standardize the treatment of patients with myocardial infarction is probably due to fear of the infrequent but unpredictable and serious complications which occur in this condition. Such standardization seems illogical, since it is increasingly apparent that myocardial infarction is a "quantitative" disease, that is, a disease in which the extent of injury, and thus the degree of severity, the frequency of complications, and the rate of fatality differ greatly. The reported rate of fatality, for instance, has varied from 8 to 83%, the discrepancy being due, no doubt, to differences in the selection of cases and in acuity of diagnosis. Recently, the use of multiple unipolar chest and limb lead electrocardiograms has made it possible to detect myocardial infarction in patients in whom the symptoms and other signs otherwise would have been inadequate for diagnosis.—John J. Sampson, M.D., *The Treatment of Myocardial Infarction, American Practitioner*, December, 1951.

THERAPEUTIC EXPERIMENTS IN FEMALE INFERTILITY

Albert Sharman, M.D., Glasgow, Scotland

The therapeutic value of uterotubal insufflation has been accepted by many writers because pregnancy has many times followed soon after the procedure.

Admittedly, the possibility of a psychological influence cannot be dismissed, and true assessment of the method is difficult. Other procedures involving instrumentation of the cervical canal, such as dilatation of the cervix and hysterosalpingography, have been known for many years to be frequently followed by pregnancy.

The *modus operandi* of "cure" by insufflation has been discussed at length by Rubin,¹ who considers it to be due to one or more of the following effects: establishing patency of the genital tract, removal of the cervical mucous plug, dilatation of the tubes, and possible psychic effect.

Until five years ago, I performed tubal insufflation routinely, both as a diagnostic and as a therapeutic procedure in all cases of primary sterility at the sterility clinic and in the wards of the Royal Samaritan Hospital for Women. Since then, the procedure has been discontinued at the sterility clinic as a routine measure, so that comparative experiments might be carried out, not only to assess the results of other methods of treatment but also to attempt a critical evaluation of the therapeutic merits of insufflation.

My insufflation cases were derived in approximately equal numbers from the clinic and from the wards. The clinic patients received no anesthesia; the others were anesthetized. A follow-up study of routine insufflation showed that, of 893 patients traced, 262 (29.3%) became pregnant. The main features of the pregnancies may be summarized as follows. A total of 158 patients were under 30 years of age, and 104 were 30 years or older when first seen. The oldest was 42 years of age and had been married for four years; she miscarried at two months. One hundred thirty-six had been married 3 years or more, 47 had been married 5 years or more, and 1, 13 years (aged 35). No patient married for a longer period than this became pregnant. Patency had been diagnosed in 231 and nonpatency in 31 cases, with 24 of the latter patients under anesthesia and the other 7 without it. All the cases of nonpatency were seen early in the series, and these patients had received insufflation once only. The fallacy of a single finding of nonpatency is apparent from these figures. Pregnancy terminated in miscarriage in 48 (18.3%) of the patients, although 7 subsequently had a full-term pregnancy; in 1 other patient, pregnancy was terminated for hyperemesis gravidarum and in another 2 for toxemia (1 at four months and the other at seven months); 1 patient had a tubal pregnancy four years after insufflation. Thus, 217 (83%) bore a child, including 2 women who bore twins. One patient had three miscarriages, and five patients had two; none of the six has since become pregnant. In 3 of the 262 patients receiving insufflation, the date of occurrence of pregnancy

could not be accurately ascertained. The time elapsing between insufflation and conception in the remaining 259 cases was as follows: 23 pregnancies occurred without an intervening menstrual period, 12 after one period, 10 after two periods, 24 after three periods, 7 after four periods, 17 after five periods, and 15 after six periods. Thus, 69 (27%) of 259 pregnancies occurred within three months and 108 (42%) within six months. During the following six months, 47 patients became pregnant. The remaining 104 pregnancies occurred at intervals varying from one to five years. Rubin² reported a series of 573 cases of primary and secondary sterility in which pregnancy occurred after insufflation. Within three months of the test, 265 (46.2%) became gravid and, within six months, 378 (64%) became pregnant.

In the first comparative series, a consecutive unselected series of 300 infertile women; the only treatment was the passing of an uterine sound. It was thought that this might throw some light on the "cervical instrumentation factor." Of the 253 patients treated and followed to date, 45 (17.7%) became pregnant within 12 months after the sound was passed; five of them missed their periods at once. In such cases, it is possible that conception preceded treatment. The pregnancies proceeded normally to term. In the other 40 pregnancies, 7 patients had only one period after the passing of the sound; 4 had two periods; 3 had three periods; 10 had four periods; 2 had five periods, and 4 had six periods. The remaining 10 had between 7 and 11 periods. An additional 11 patients became pregnant more than a year after the passage of the sound, 6 of them without any further form of treatment and 5 after tubal insufflation.

I followed this study with one of a similar, consecutive series of 300 patients with primary sterility in whom nothing more was done than a bimanual pelvic examination at the first visit to the sterility clinic. To date, 286 patients have been traced, of whom 31 became pregnant (10.8%); nine of them missed their periods at once. In the other 22 pregnancies, 6 patients had only one period after examination, 3 had two periods, 6 had three periods, 3 had four periods, and 2 had six periods. The remaining 2 had 9 and 11 periods respectively. In addition, two patients became pregnant more than a year after examination but after the subsequent passing of a sound.

The next series planned was a similar, consecutive series of 300 patients with primary sterility who were given intramuscular injections of "disecron" (injection containing 2.5 mg. of estradiol monobenzoate and 12.5

From the Royal Samaritan Hospital for Women.

Read before the Section on Obstetrics and Gynecology at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 14, 1951.

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mg. of progesterone in 1 cc. ethyloleate) over a period of six months. The injections were given every third day, commencing with the fifteenth day of the menstrual cycle as the presumptive date of ovulation until the onset of menstruation, or if the latter did not supervene, for two more weeks until a Friedman test could be performed. The preparation, made by the British branch of the Schering Corporation, is a sterile oily solution, containing 12.5 mg. of progesterone, with 2.5 mg. of estradiol benzoate (estradiol monobenzoate). The formula has been "modelled upon a method of treatment originated by Zondek." The theoretical basis for its use is that an important cause of female infertility is the failure of nidation of the fertilized ovum because of incomplete preparation of the endometrium. It is also suggested that, even though nidation occurs in some cases, the level of circulating hormones produced by the corpus luteum is inadequate to maintain pregnancy, with the result that abortion occurs at so early a stage that it may be considered as a form of sterility. The "disecron" series is as yet incomplete, 243 patients having been treated to date. In 203 patients, sufficient time has passed to endeavor to assess results; however, owing to the many attendances required and, in several cases, owing to aversion to per-

cron" group will be reckoned as treated from the start of the series of injections. The most important comment is that three of the groups were small. Pregnancy supervened within 12 months in 17.4% of the insufflation group, 17.8% of the "sound" group, 10.8% of the "nothing done" group, and 19.6% of the "disecron" group. These figures show a decisive advantage in the three actively treated groups for the year of the follow-up (see the table).

When these figures are further analyzed, one finds that, in the first three months, the pregnancy rates were fairly uniform, ranging from 6.9% in the "disecron" group to 8.4% in the "nothing done" group. (The "nothing done" group may have shown better results owing to the fact that nine women conceived after treatment without any supervening menstruation). The advantages of the active measures were not apparent until the fourth month but then continued until the end of the year. Most notably, the "disecron" group had a pregnancy rate of 11.3% from the fourth to the sixth month inclusive, after the commencement of treatment. On the other hand, only two pregnancies occurred in the "disecron" group after completion of the six month "course."

The investigations permit us to compare two moderately large groups, the 893 patients treated by insufflation and the 682 others. The pregnancy rates in these two groups were virtually identical in the first three months, and they differed little even at the end of the year, being 17.4% and 15.3% respectively. Although in this respect the insufflation group showed only a slight advantage, it must be borne in mind that the chief value of insufflation is diagnostic.

A psychological effect was possible in all four groups, even in the "nothing done" group there was the fact of medical intervention, and these patients understood that they were receiving expert medical care. In order to consider further any psychological effect of medical intervention, one would have to compare the incidence of pregnancy in a group such as our bimanually examined patients with the incidence in a group of previously sterile but not medically attended patients. The sterility of an unattended group would either be inferred from childlessness or rest on answers to interrogation. On the other hand, the evidence for the previous sterility of sterile patients always includes the fact that they have found it necessary to seek medical advice. Thus, the two groups are not strictly comparable.

Even if one ignores the psychological factors, the difficulty of obtaining comparative figures regarding untreated sterile women remains; the best alternative to the study of a group such as the series of patients who were only bimanually examined. Some clinicians have concluded that pregnancy frequently soon follows bimanual examination of sterile patients; however, this method has not yet been adequately assessed. Whether or not this particular procedure proves worth continuing, the comparison of results is the best if not the only way to assess methods of treating sterility. The most important requirement for such comparisons is that the groups compared are large; the present communication is chiefly intended as a contribution to future compilations, extensive enough to minimize the effects of chance.

Pregnancy Percentage Rates in Groups of Sterility Cases

No. of Periods After Treatment	Insufflation Group (893 Patients)	Uterine Sound Group (253 Patients)	Bimanual Examination Group (286 Patients)	Hormone Therapy Group (113 Patients)
0-3.....	2.6	2.0	3.1	1.4
0-6.....	7.7	7.5	8.4	6.9
0-12.....	12.1	13.8	10.4	18.2
0-12.....	17.4	17.8	10.8	19.6

cutaneous injections, the default rate was high. Of 28 patients successfully or adequately treated and 28 became pregnant (19.6%) within 12 months after the commencement of "disecron" injections. Two of them missed their periods at once. In the other pregnancies, 3 patients had only one period commencing "disecron" treatment; 3 had two periods; 2 had three periods; 4 had four periods; 7 had five periods; and 5 had six periods; the remaining 2 had nine periods each.

The husbands of the patients in all the groups were referred for seminal examination at the first interview with the patient; this examination was carried out in 47% of the 1,575 cases. In the husbands of the patients who had insufflation, seminal examinations showed major impairment in 25.1% and total azoospermia in 12.4%. The corresponding figures were 20.7% and 6% in the "uterine sound" group, 26.8% and 6% in the "nothing done" group, and 26.7% and 9.4% in the "disecron" group. The experimental groups also appeared to warrant comparison with each other and with the insufflation series, on the grounds of being unselected and of being statistically similar in respect to age distribution and duration of marriage.

RESULTS

In analyzing the results, I will not go beyond one year, which was the limit of the follow-up period in one of the groups. For the purpose of analysis, the "dis-

In view of present knowledge, it appears advisable to combine diverse methods of treatment that appear relatively useful when employed separately. In view of the findings reported above, the combination of insufflation with hormone therapy deserves consideration. In this connection, one would welcome new preparations of hormones for oral administration, for these would do much to lessen the defaulting that has been noted among patients requiring repeated injections.

The intervention of chance in individual cases is well known, but I venture, in conclusion, to add a few instances of some salutary successes. In one case, a sound was passed in a 37-year-old woman, married five years. Insufflation was done eight months later. A cervical polyp was removed one year after insufflation. She became pregnant at the age of 40, a month after adopting a baby. In another case, an endometrial biopsy was performed in a 31-year-old woman, married three years. Two insufflations were done in the next two months. A

sound was passed two years after the insufflations. A cervical erosion was cauterized a year later. She became pregnant two years after the cauterization. In a third case, a 31-year-old woman married six years had an insufflation. Endometrial biopsy was performed three years later and a sound was passed five months after that. Insufflation was repeated two years later. After no further treatment for two years, she became pregnant.

SUMMARY

A total of 1,575 primary sterility patients were followed for 12 months, 893 after insufflation, 253 after the passing of a uterine sound, 286 after bimanual examination, and 143 after commencing injections of progesterone combined with estradiol benzoate. The pregnancy rates at the end of three months were fairly uniform (6.9% to 8.4%); at the end of the year the rates were respectively 17.4, 17.8, 10.8, and 19.6%. Larger comparative compilations are required to ascertain the validity of the results.

REVIEW OF MASS CHEST X-RAY SURVEYS

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As the community-wide chest x-ray survey has developed in recent years, it has become, today more than ever, a concentrated attack on tuberculosis. Through the use of the photofluorograph, we now screen entire communities—the adult population of whole cities or large metropolitan areas—and, in so doing, find tuberculosis and gather the information we need to build more effective tuberculosis control.

In the achievement of these purposes, the community-wide chest x-ray survey is based on a blending together of the efforts of all the resources, skills, interests, and knowledge of an entire community. This blending together of resource and effort becomes apparent even before the photofluorographic units begin their screening operations. It becomes apparent in the modification of local tuberculosis control resources and practices to meet the special needs of the survey—in the provision of special laboratory services to aid the physician in the essential task of diagnosis, in the provision of special nursing and social work services in support of medical follow-up efforts, and in the expansion of treatment facilities to care for the cases found in the survey.

Out of the alloy of professional and public interest and effort that the community-wide survey represents, there has been forged in every locality where such programs have been undertaken an effective tool for tuberculosis case finding. The essence of the amalgam has been the leadership of the practicing physician and the medical society.

In the last four years, the United States Public Health Service has participated in 14 community-wide chest x-ray surveys. In so doing, it has aided in the small-film screening of nearly 5½ million persons from one end of the country to the other.

At the time that the Public Health Service made its decision to assist communities of over 100,000 popula-

tion to conduct mass chest x-ray surveys, it was recognized that the x-ray had limitations as a diagnostic tool for tuberculosis. Some of these limitations stem from the variability of interpretation, while others arise from the variable patterns of the disease itself and from our lack of fully definitive knowledge of the disease process. As we know so well, a two-dimensional shadowgraph of the chest is not a perfect means for finding thoracic disease. Some infiltrates and, as a matter of fact, some cavities are subtle in appearance and difficult to distinguish. But the many unsuspected lesions that had been brought to light in limited mass surveys represented compelling reasons for enlarging the scope of tuberculosis case finding. The Public Health Service therefore embarked on its program to assist certain localities in x-raying persons over the age of 15.

At the same time, however, in an effort to cast some light on the question of the precise value of the mass survey to tuberculosis control—and to learn how to minimize the x-ray's limitations—the Public Health Service set up two research facilities to be conducted concurrently with actual mass survey operations. One of these, which was set up in Muscogee County, Georgia, was designed to study the occurrence and spread of tuberculosis within a community following an intensive case-finding program. The other, which was organized as the Central Cooperative Clinic in Philadelphia, aimed to follow the health histories of tuberculosis suspects found in industrial surveys. Both these research facilities had the over-all purpose of providing the knowledge for sharpening and refining mass survey operations.

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Although it was recognized at the outset that the findings in one community are not applicable to all communities, Muscogee County, which includes the city of Columbus, was selected as the over-all check-plot base for studying the effects of mass x-ray surveys. It is already apparent from this particular study—where, by the way, we now have survey information to correlate with tuberculin sensitivity findings and general tuberculosis mortality information—that the immediate effects of a chest x-ray survey may depend, to some extent, on the importance of endogenous disease that becomes active within a community after a screening program.

In the three and a half years following the initial screening program, average annual death rates appear to be about the same for both the group that received x-ray examinations and the group that did not. Superficially, then, it might seem that the survey had no effect on the death rate of those participating in the survey. But, if we assume that early detection, isolation, and treatment in tuberculosis do prevent death from the disease—an assumption that we must make if we are to have a basis for our control efforts then we must conclude that the survey did reach the more critical or more vulnerable portion of the population. Without the screening program, death rates for the group actually surveyed would perhaps have been higher.

Certainly, the prompt isolation of the infectious cases revealed by the x-ray survey must have had some effect on the spread of the disease by limiting the incidence of new exogenous infections and exogenous reinfections. The true effects of the x-ray survey and its follow-up may therefore be masked, to some extent, by the amount of silent and invisible endogenous disease that existed in the community. Obviously, the whole question of the relationship of exogenous and endogenous infections and their relative importance need elucidation before the exact value of a chest x-ray survey can be assayed.

Clarification of this enigma of the nature of tuberculosis, perhaps, also shed some light on the occurrence of 25 postsurvey deaths among persons whose survey roentgenograms, even in retrospect and with knowledge of the exact location of the fatal lesions, were clearly and indisputably free of any indication of tuberculous disease. In this connection it is important to note that, of the 25 who died, 3 were white and 22 were Negro.

In the three and one-half years following the survey, the average annual tuberculosis death rate for the entire population was 34.0 per 100,000. For the white population it was 17.5 per 100,000, while for the Negroes it was 72.4. In contrast, the death rates for those with negative initial survey roentgenograms were 3 per 100,000 for whites, as against 39 for Negroes. In other words, the death rate for the Negroes was 13 times that for the whites. This, in spite of the fact that case finding coverage among the Negro population of Muscogee County was more nearly complete than among whites.

For the white population, the Muscogee County experience indicates that case finding and subsequent medical supervision appear to meet the problem of those who might otherwise die of tuberculosis. For the Negroes, however, it would appear that resurveys at frequent intervals—or, at least, more frequent and more intensive

case finding of some sort—is highly desirable if they are to benefit by early discovery of the disease.

It must be admitted, however, that there is no clear indication of the best approach to the problem. Having identified the especially vulnerable group, should we address our subsequent case-finding efforts toward that specific group, or toward the entire population that contains that group? Continued analysis of information from such programs as the Muscogee County study, as well as those from the operating programs in the various cities themselves should provide the knowledge we need to answer this question and to increase the value of mass case finding as a tuberculosis control tool.

Detailed findings from the surveys in which we have participated are of interest as they relate to the coverage they achieve and the amount of disease they bring to light. In the first stage of survey operations—that is, the small-film screening examination—coverage in the 14 community-wide programs to date has varied from place to place. The goal of screening operations is usually set at 80% of the eligible population 15 years of age and over. In actual operations, total small films taken range between 55% of this eligible population (in St. Paul, Minn.) and 93% (in Salt Lake City).

Generally, the two sexes respond more or less equally. Response by race, however, is varied from one city to another—in Denver, screening coverage for nonwhites was far below that for the white population. There, 42% of the Latin-American population and 61% of the Negroes were screened, as against 77% of the white population. In Washington, D. C., on the other hand both whites and nonwhites had more or less equal coverage.

It has been our experience that the older age groups do not usually respond to small-film operations as well as the younger population groups. In the Seattle survey which was held in 1948, the response ranged from a high of 84.2% in the 15-24 year age group to a low of 35.8% for those 65 years of age and over. Similarly, in the Cleveland survey (1949) coverage ranged from 74.5% in the 15-24 age group to 35.3% for persons 65 and over. These percentage-coverage figures represent, at this time the usual range of expectancy for small-film screening programs.

In the second stage of survey operations—confirmatory 14 by 17 inch films for those with suspicious small film findings—our experience has been as follows: First we have found that between 2% and 7% of those screened by small-film examination will need confirmatory 14 by 17 inch films. Of those recalled for confirmatory films, between 80% and 95% have actually responded.

Of the total number of 14 by 17 inch films taken in the 14 community-wide surveys to date, the total prevalence of findings suspicious of tuberculosis have ranged from 0.6% of all persons receiving small-film examination (for Salt Lake City) to 2% (for Maricopa County, Arizona, preliminary information). In two surveys, Seattle and Cleveland, the prevalence of 14 by 17 inch film findings suspicious of tuberculosis were tabulated by census tract, as a means of indicating the correlation between these findings and socioeconomic status. The information appears to confirm the commonly held notion that tuber

culosis prevails to a greater extent at the lower socioeconomic levels. In Seattle, the lowest "income" group experienced a prevalence rate of 13.7 suspicious large films per 1,000 persons examined, while the highest level showed a rate of 10.7 per 1,000. In Cleveland, the same general pattern is apparent, with a rate of 9.2 per 1,000 for the lowest economic level and 6.2 for the highest.

In most surveys, referral to private physicians or public clinics occurs immediately after the confirmatory large films are taken and read. In some, however, further diagnostic study is undertaken before a referral is made. This was the case in the Denver survey, where a diagnostic center was established as part of the survey organization in an effort to furnish the practicing physician to whom the patient was to be referred with as much pertinent diagnostic information as possible. The Center was staffed by local physicians, and patient referrals were made after the tentative diagnostic study indicated the need for long-term supervision.

In all of the surveys, suspects are referred to private physicians of their own choice or to public clinics, depending, in general, on their ability to pay for medical care. To date, referrals have been made to private physicians for about 80% of the suspects found, while some 20% have been referred to public clinics. In the Denver survey, 73% of all tuberculosis cases—including active, inactive, and questionably active—were sent to private physicians, while 23% were sent to public clinics. For those with active tuberculosis, the proportion choosing clinic follow-up was higher.

Since the principal aim of mass chest x-ray surveys is to find significant tuberculosis in the screened population, the question of how much active tuberculosis is found is fundamental. Although reporting by private physicians has not been complete, or diagnostic methods and criteria uniform, the information we have assembled indicates that about one out of every 1,000 persons screened will have active tuberculosis that is clinically recognizable. Our experience indicates, too, that many of those found with inactive and questionably active disease will later prove to have definitely active tuberculosis.

Moreover, as we have found from a detailed analysis of five surveys, about 85% to 90% of the active cases are unknown to the health department. The identification of these previously unknown cases of active tuberculosis represents one of the major contributions of the community-wide survey wherever it is held.

Although tuberculosis is the primary concern of community-wide chest x-ray surveys, the screening programs do identify other pathological conditions of the chest, including thoracic neoplasms and cardiovascular abnormalities. In view of our aging population, this is assuming greater value as a by-product of tuberculosis case-finding projects. In the Boston survey, which was held in the latter part of 1949, special procedures were instituted for the follow-up of tumor suspects found in the screening program. A roentgenologic review board was organized to read the 14 by 17 inch chest x-rays and to identify all findings suggestive of thoracic neoplasms. After the radiological interpretations, all suspects were referred to a medical social worker for help in obtaining medical follow-up either under the supervision of private physicians in the area or in public clinics. According to

Dr. C. L. Scamman, a total of 76 cancer neoplasms were found, of which 43, or well over half, were of the primary type. Furthermore, most of the cancers found were discovered at a time when they were most likely to be resectable.

For the 43 cases of proved primary cancer, the total time required to identify them—an all-important factor in their control—was relatively brief. As a matter of fact, the total time that elapsed between the time the small film was taken and the establishment of a final diagnosis averaged approximately 56 days.

As one would expect, the Boston survey found a direct correlation between the prevalence of cancer and age. Except for the oldest age group examined—where incidentally, the number of persons screened was extremely low—the total number of cancer cases found was greater in each successive age group. As one would expect, too, more neoplasms were found among men than among women.

In this same survey in Boston, special procedures were also established to identify the cases of cardiovascular abnormalities among the population screened. Observations on this subject are now undergoing intensive analysis, and findings will be published in the near future. In our experience, readings of cardiac abnormalities have appeared in 2 to 10 x-rays of every 1,000 taken in community-wide surveys. Since information on the follow-up of cardiac suspects is scanty, it is difficult to estimate the effects of the identification of those with possible cardiovascular disease. There are rather divergent views regarding the value of the x-ray in finding cardiovascular disease that can be benefited medically. Findings from the special study in Boston, it is hoped, will help to resolve these divergent views.

Just as the Boston survey has made cancer and heart disease studies possible, so does every community-wide survey provide the opportunity for studying tuberculosis and tuberculosis control efforts. In some areas, physicians to whom suspect cases have been referred have done a thorough job of diagnostic study and patient follow-up and have reported back to the survey organization consistently and in detail. Wherever this has occurred—where physicians have conducted complete follow-up on all referred suspect cases and have reported to the survey organization—the structure of knowledge about tuberculosis is being built up and control programs are being modified to conform with the knowledge gained. With the survey's stimulus and the increase of public interest in and support for tuberculosis control, improvements in the program have been made possible in many places.

In Denver, for example, several tuberculosis control program improvements can be directly attributed to the impact of the community-wide survey. First, more funds are now available for the care of tuberculosis patients—to the extent of about 50%. Personnel has been increased, photofluorographic equipment has been purchased, and the entire, official control program has been expanded.

In Salt Lake City, the survey brought with it a tuberculosis case register, a device that had not existed there prior to the survey. In Seattle, hospitalization of tuberculosis patients rose to 4.3 patients per annual death.

CONCLUSION

In our experience with community-wide chest x-ray surveys, over the past four years, we have learned, that, despite the x-ray's limitations, the mass survey has positive value in the discovery and consequent control of

tuberculosis. As our research programs in mass radiography—and our operating programs—progress in the future, we can expect that the mass approach to tuberculosis case finding will make even greater contributions to the fight against tuberculosis in the United States.

TREATMENT OF PULMONARY ACTINOMYCOSIS WITH CHLORAMPHENICOL

REPORT OF A CASE

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and

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Actinomycosis was first described in the cervicofacial form in cattle by Bollinger¹ in 1877. His botanical colleague, Harz,² observed the radiate formation of the micro-organism, and applying the term "actinomyces" from the Greek to connote "ray-fungus," named the disease "actinomycosis." It was not until the following year, however, that the first case of actinomycosis in a human being was reported by Israël.³ By 1885 he had accumulated data on 38 cases, and had written the first comprehensive, clinical description of the disease in man.⁴ Together with Wolff⁵ in 1891, he described the etiologic agent and its anaerobic growth in detail.

Until the appearance of the sixth edition of "Bergey's Manual of Determinative Bacteriology"⁶ in 1948, numerous investigators held the opinion that actinomycosis in cattle and man was caused by the same anaerobic micro-organism, and, depending on the investigator, called it either *Actinomyces bovis* or *Actinomyces israeli*. The former statement appeared as fact in the latest editions of textbooks of bacteriology and mycology. Presumably based on the work of Erikson,⁷ "Bergey's Manual" catalogues *Actinomyces israeli* as the cause of

actinomycosis in human beings, and *Actinomyces bovis* as the etiologic agent of the bovine disease. Erikson's opinion that there are two distinct cultural types of anaerobic *Actinomyces* was amply supported in 1944 by the work of Thompson⁸ at the Mayo Clinic.

Through the efforts of numerous investigators, such as Wolff, Israël, Sullivan, Goldsworthy, Lord, Naeslund, Emmons, Slack, and Rosebury, it has been established clearly that the anaerobic *Actinomyces* is a frequent, not normal, inhabitant of the oral cavity and respiratory tract and rarely is found as a free saprophyte. Infection in man is endogenous in origin, therefore, rather than exogenous, as has been the popular belief for many years.

The disease is usually initiated by the disruption of the normal barriers to infection by trauma or following a disease process. Thus, cervicofacial actinomycosis may follow tooth extraction, periodontitis, or severe dental caries; while abdominal actinomycosis may appear several weeks or months after an acute, perforative gastrointestinal disease, such as acute appendicitis, perforated colonic diverticulum, perforated peptic ulcer, acute ulcerative disease of the intestinal tract, or after trauma. Pulmonary actinomycosis is likely to appear in persons with poor dental hygiene following aspiration of actinomycetes-infected material from the mouth, since the organisms are normally harbored in great numbers in pyorrheic gums, carious teeth, and tonsils. Actinomycotic pneumonia may result, with pleural invasion and the ultimate formation of multiple, draining thoracic sinuses which are extremely difficult to treat and eradicate. It is also realized now that actinomycosis in its various forms is as common in urban as in rural areas.^{9a}

Although numerous forms of therapy have been employed successfully for cervicofacial actinomycosis, they have proved to be of less value in the management of the more grave pulmonary and abdominal forms. Some of the therapeutic agents have been iodides, copper or iron salts, gold preparations, thymol, arsphenamine, vaccine and radiation. Surgical treatment has consisted of repeated excision and curettage. With the introduction of sulfadiazine for actinomycosis in 1937,¹⁰ and penicillin in 1943,¹¹ a new therapeutic era for this disease was opened and the prognosis was vastly improved. By 1944 penicillin therapy for actinomycosis was firmly established.

Miss Marian Schoenherr assisted in some phases of the laboratory work.

From the Thoracic Surgical Section and Laboratory Service of Walter Reed Army Hospital.

Some of the illustrations have been omitted from THE JOURNAL; they will appear in the authors' reprints.

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lished.¹² In 1950 aureomycin was added to the armamentarium by McVay and co-workers,¹³ who successfully treated one case of cervicofacial actinomycosis with this antibiotic.

Meanwhile, chloramphenicol (chloromycetin®) was discovered in 1947,¹⁴ and its antibiotic activity demonstrated. Then in 1949, McLean and co-workers,¹⁵ studying the in vitro susceptibility to chloramphenicol of a large variety of micro-organisms, noted that one strain of *Actinomyces bovis* was inhibited by 5 γ per milliliter. We extended this observation to *Actinomyces israeli* the following year,¹⁶ and we discovered that six strains of the micro-organism, all isolated from patients with actinomycosis, were inhibited in vitro by concentrations of antibiotic ranging from 1 to 3 γ per milliliter. On the basis of this marked in vitro sensitivity, a clinical trial of chloramphenicol in the treatment of actinomycosis was recommended.

REPORT OF A CASE

W. P., a white man aged 46, had increasing difficulty with pyorrhea and abscesses of the gums in 1948 and 1949, necessitating extraction of four upper canine and incisor teeth in July, 1950. In October he began to experience intermittent sharp, right upper abdominal pain, unrelated to food intake, which radiated around to the back and up to the right scapula, and, in addition, pain in the right chest at the level of the fourth anterior rib. He became moderately dyspneic and produced a foul-tasting but scanty greenish-yellow sputum. Since treatment in his locality for cholecystitis had been unsuccessful, the patient sought hospitalization at Walter Reed Army Hospital, where initial roentgenograms of the chest were interpreted as marked enlargement of the right side of the heart. Shortly afterward, he expectorated large quantities of foul-smelling greenish-yellow sputum. Sub-



Fig. 1.—Roentgenogram of chest taken Nov. 13, 1950, reveals a localized, localized actinomycotic empyema cavity, of an estimated capacity of 350 cc., within the right lung.

sequent chest fluoroscopy and roentgenograms showed the "cardiac enlargement" to be a partially emptied cyst, located in the right, medial posterior lung field and probably within pulmonary tissue (Fig. 1). At operation two months later, however, the remains of the "cyst" proved to be a localized, loculated empyema cavity contained entirely within the pleural space and not encroaching on pulmonary parenchyma.

Physical examination revealed a tall, chronically ill, white man with a temperature of 102 F. A blood pressure of 133 systolic and 82 diastolic, a pulse rate 82 per minute, and a respiratory rate of 18 per minute, who had exceedingly foul breath, pyorrhea alveolaris, severe dental caries and periodontoclasia, cheilosis of the oral commissures and a smooth red tongue indicative of nutritional deficiencies, a slightly enlarged liver but



Fig. 2.—Lateral roentgenogram demonstrates the size and extent of lipiodol-injected empyema cavity.

no abdominal tenderness, lungs which were clear to auscultation and percussion, and occasional premature auricular beats but no enlargement of the heart by percussion.

On the day of admission, Nov. 18, 1950, the empyema cavity was aspirated through the eighth right posterior intercostal space, yielding 300 cc. of thick, extremely foul-smelling, greenish yellow pus, microscopic examination of which showed masses of gram-positive, non-acid-fast, slender, branching rods resembling *Actinomyces*, gram-positive streptococci, and fusiform bacilli. Cultivation of the pus yielded *Actinomyces israeli*, anaerobic streptococci, and anaerobic fusiform bacilli. No aerobic organisms were recoverable from this foul material. Lipiodol® (an iodized oil used as a contrast medium) instilled into the cavity appeared on chest roentgenogram behind the right leaf of the diaphragm but not involving it and extending low into the posterior portion of the lung field (Fig. 2). The patient tasted lipiodol® shortly afterward, indicating the presence of a bronchopleural fistula. The strain of *Actinomyces* isolated was sensitive to 3 γ chloramphenicol per milliliter which was within the "very sensitive" range reported for six other pathogenic strains,¹⁶ while the anaerobic *Streptococcus* was sensitive to 1 γ per milliliter.

The white blood cell count was 16,200 per cubic millimeter, with a differential cell count of 89% polymorphonuclear leucocytes, 9% lymphocytes, and 2% monocytes. The red blood cell

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count was 5 million per cubic millimeter, and the hemoglobin value was 13.9 gm. Prothrombin time was 16 seconds, the normal laboratory base line for this and subsequent determinations being 15 to 16 seconds. The sedimentation rate (Wintrobe) was 30 mm. in 60 minutes, corrected. Blood urea nitrogen was 15 mg. per 100 cc.; total serum protein, 6.4 gm. per 100 cc.; serum albumin, 2.9 gm.; and serum globulin, 3.5 gm. The urine was

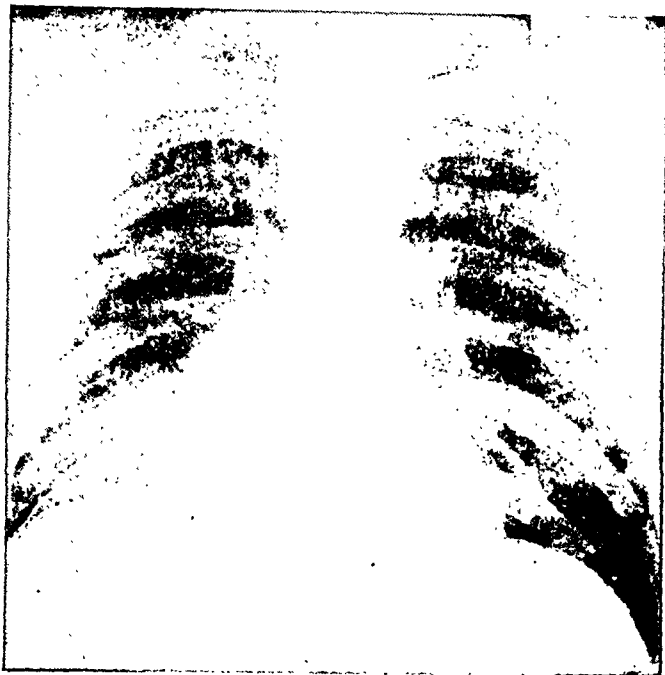


Fig. 3.—Roentgenogram of chest taken Nov. 24, 1950, after six days of chloramphenicol therapy demonstrates reduction in the size of the cavity.

essentially normal. Coccidioidin 1:100, blastomycin 1:100, histoplasmin 1:100, and first and second strength intradermal tuberculin tests (purified protein derivative) were negative.

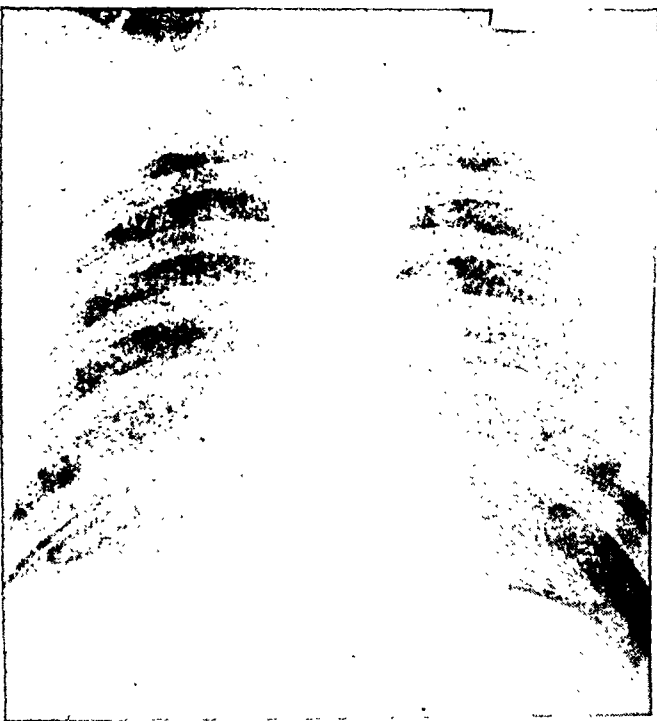


Fig. 4.—Roentgenogram of chest taken Dec. 28, 1950, following 40 days of continuous chloramphenicol therapy and two local instillations of crystalline antibiotic reveals obliteration of the empyema cavity and the presence of residual lipiodol.®

Chloramphenicol therapy was instituted in doses of 750 mg. orally every four hours, supplemented by two successive instillations into the empyema cavity of 2 gm. of sterile crystalline chloramphenicol (supplied by Parke, Davis & Co., Detroit, Mich.), suspended in 10 ml. of isotonic saline. Daily intramuscular injections of vitamin B complex, oral multivitamins, and a high protein, high caloric diet were prescribed. The pa-

tient's temperature returned to normal by the fourth day of therapy, and the contents of the empyema cavity were reduced in volume to 65 cc. of thin, nonodorous, sterile material at the third aspiration (Fig. 3). The fifth and all subsequent attempts at thoracentesis failed to yield any pus. Serial roentgenogram of the chest demonstrated progressive diminution of the size of the cavity until Dec. 28, 1950, when the right lung field was entirely clear, save for residual lipiodol® in the pleural space (Fig. 4). The patient was referred to the dental clinic, where eradication of focuses of infection was recommended. All of the patient's teeth were then removed while he continued to receive chloramphenicol. Cultivation of the scrapings of the extracted teeth yielded *Actinomyces israeli*, as well as many other mouth organisms. The patient was given a short convalescent leave, during which time the oral daily dose of chloramphenicol was reduced to 2 gm. (Fig. 5).

On Jan. 10, 1951, after 53 days of continuous chloramphenicol therapy, a right thoracotomy was performed with the patient under gas-oxygen-ether anesthesia with resection of the seventh

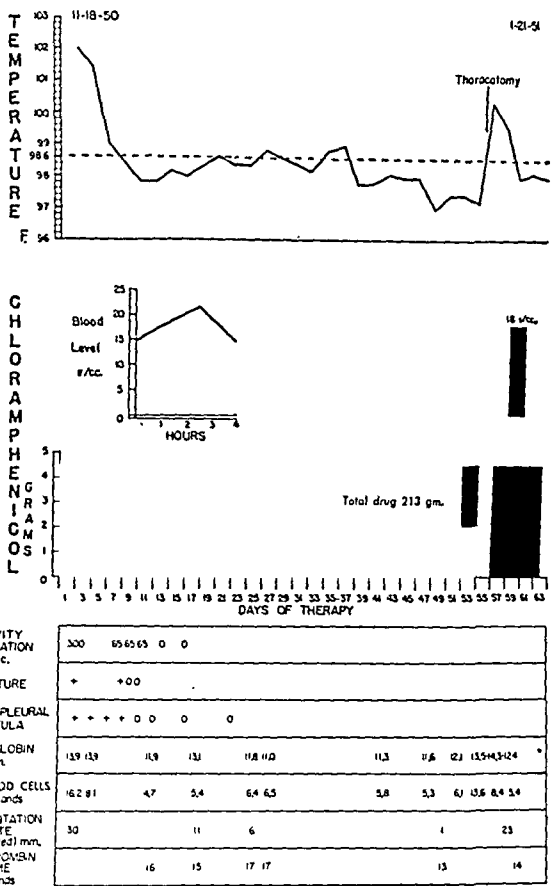


Fig. 5.—Chart showing response of a man aged 46, who weighed 182 (82.7 kg.) and who had actinomycotic empyema of the right lung, chloramphenicol.

rib. When the chest was opened, the right lung was completely adherent to the chest wall by filmy, easily separable adhesions and in the posterior gutter, at the level of the eighth, ninth, and tenth ribs, by dense adhesions, the latter representing the remains of the actinomycotic empyema cavity as seen in the roentgenograms (Fig. 1 to 4). The lung was freed from the chest wall, except in this firmly attached area. Extrapleural resection was elected as the procedure of choice. The encapsulated cavity measuring 5 by 3 cm. and containing 4 to 5 cc. of thick, yellowish, nonodorous fluid which later proved to be sterile, was moved from the lung and chest wall by sharp dissection. Upon reinflation of the lung, several tiny air leaks which appeared on the posterior surface of the right lower lobe were closed with absorbable gelatin sponge (Gelfoam®) placed between it and the parietal pleura. A posterior drain was placed in position, and the chest was closed in layers in the usual manner. The patient tolerated the procedure well.

Pathological examination of the cavity wall revealed highly vascular granular tissue, areas of suppuration and fibrosis, microabscesses, and giant cells, a tissue reaction compatible

with that of actinomycosis. Several granules were seen in various sections but they did not contain any branching organisms.

The patient's postoperative course was uneventful, and he was discharged on the 10th postoperative day with a completely reexpanded clear right lung, asymptomatic and afebrile (Fig. 6). A letter from him in May stated that he was in good health.

BACTERIOLOGY

The traditional and cumbersome technique of deep veal infusion agar cultivation for the isolation of pathogenic anaerobic actinomycetes as recommended in many standard textbooks is unnecessary, since the micro-organism grows readily in surface colonies on suitable agar medium, and may therefore be isolated in the pure form by simple bacteriologic techniques.

Actinomycotic exudates are streaked over (1) several bacto® brain-heart infusion agar plates containing 0.5% dextrose and planted into (2) thioglycollate glucose broth (Brewer's anaerobic medium). The plates are incubated for four to six days at 37 C. in a Brewer anaerobic jar with 5 to 10% added CO₂. Although many bacterial species thrive under anaerobiosis on the brain-heart infusion dextrose agar, colonies of *Actinomyces israeli* are so distinctive that, with a little experience, one may easily detect their presence. They are tiny, only 1 to 3 mm. in size, and appear starchy white, although some strains are slightly yellow or greyish. The surface of the colony glistens under reflected illumination and has an irregular and contoured surface very much like the crown of a molar tooth.¹⁷ The colony is adherent to the agar and is difficult to emulsify, often coming away from it in one piece and leaving a pitted



Fig. 6.—Roentgenogram of chest taken Jan. 19, 1951, nine days post-operative, reveals a missing seventh right rib, some elevation of the right diaphragm, residual lipiodol, ⊗ and some pleural thickening, but essentially clear lung fields.

area. Microscopic examination reveals a loose aggregate of branched gram-positive, non-acid-fast, long slender rods (Fig. 7).

Colonies of *Actinomyces bovis* under anaerobiosis on the same agar medium vary in size from 1 to 2 mm., are

also starchy white, but do not have the roughened appearance of *Actinomyces israeli*, and are considerably easier to emulsify. Furthermore, pure culture growth of the micro-organism in thioglycollate medium is diffuse, while that of the human pathogen is discrete, in the form of compact granules, irregularly round and

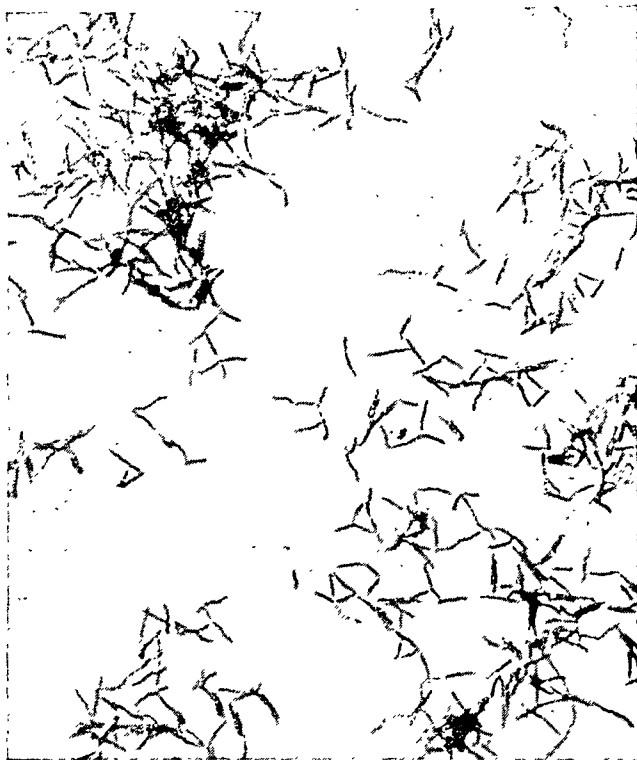


Fig. 7.—*Actinomyces israeli*, gram stain, $\times 1,400$.

of variable size, usually found below the oxygenated zone of the medium.

Primary tubes of thioglycollate medium are incubated four to seven days at 37 C., and finely drawn Pasteur pipettes are employed to fish out suspicious colonies of micro-organisms. These are streaked over bacto® brain-heart infusion dextrose agar and placed under anaerobiosis with added CO₂. Although pathogenic, anaerobic actinomycetes grow in liquid thioglycollate medium at a rate slower than those of the usual ubiquitous secondary micro-organisms; they appear in sufficient numbers in four to seven days to permit their isolation in pure culture. Other organisms besides *Actinomyces israeli* which form balls or colonies in liquid thioglycollate medium are various species of anaerobic streptococci.

Pure strains of pathogenic, anaerobic actinomycetes isolated by one of us (M. L. L.) in the past from various patients with actinomycosis required either limited oxygen atmosphere in anaerobic jar or reduced oxygen tension in thioglycollate medium and have consistently failed to grow aerobically. This coincides with the experience of other workers.¹⁸ Although a small percentage of strains of actinomycetes are reported to be capable of scant

17. Sullivan, H. R., and Goldsworthy, N. E.: A Comparative Study of Anaerobic Strains of Actinomycetes from Clinically Normal Mouths and from Actinomycotic Lesions, *J. Path. & Bact.* 51: 253-261 (Sept.) 1940.

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growth under aerobiosis,¹⁹ the majority thrive best under anaerobic or microaerophilic states.

Pathogenic anaerobic actinomycetes are to be differentiated from the aerobic *Nocardia asteroides*, a pathogenic, partially acid-fast, gram-positive, branching rod which does not produce the typical actinomycotic granule in tissue and is the agent of nocardiosis, a tuberculosis-like disease of high mortality. The confusion in the nomenclature of the etiologic agents of actinomycosis and nocardiosis was clarified in 1943 by Waksman and Henrici.²⁰ *Nocardia asteroides*, growing aerobically on brain-heart infusion dextrose agar, produces small, orange-yellow colonies, the surface of which becomes powdery with age owing to fragmentation of the mycelium into rod-shaped conidia.

Actinomyces bovis may be confused easily with anaerobic or microaerophilic diphtheroids. However, the latter organisms are, for the most part, nonpathogenic to mice on intraperitoneal inoculation with mucin,²¹ or, if pathogenic, they fail to produce the typical actinomycotic tissue lesion. They grow much more rapidly than actinomycetes in both fluid thioglycollate medium and anaerobic brain-heart infusion dextrose agar, visible growth appearing within 24 to 48 hours, diffusely in thioglycollate medium, and in greyish, butyrous, easily emulsifiable colonies in the latter medium.

In vitro sensitivity of *Actinomyces israeli* to chloramphenicol was determined by the method of Littman, Phillips, and Fusillo,¹⁶ while serum chloramphenicol levels were assayed by the technique of Smith, Landers, and Forgacs.²² Plates of thioglycollate agar seeded with 400,000 spores per milliliter of *Bacillus subtilis* received 4 small metal cylinders containing patient's serum. After incubation of the plates, cleared zones produced by the patient's serum were compared with those obtained with standard concentrations of chloramphenicol and the level computed.

COMMENT

The favorable response of only one patient to chloramphenicol therapy could hardly be used as a basis for a conclusive statement concerning the clinical effectiveness of this antibiotic for pulmonary actinomycosis. It does, however, serve to point out that additional clinical evaluation of chloramphenicol for this and other forms of actinomycosis is worthwhile, especially when reports exist of the inadequacy of combined penicillin and sulfadiazine therapy for permanent cure of some patients with pulmonary actinomycosis,²³ and the inadequacy of penicillin in controlling anaerobic streptococci which frequently coexist with actinomycetes in pulmonary lesions. It also demonstrated to us the feasibility of instilling crystalline chloramphenicol into an empyema cavity with apparent minimal reaction.

Because of the chronicity of pulmonary actinomycosis, which is characterized by periods of remission and exacerbation, a prolonged period of chloramphenicol therapy was thought to be necessary, as is customary with penicillin and sulfadiazine treatment. The patient received a total of 213 gm. of chloramphenicol in continuous therapeutic doses over a period of 64 days. Although a relative neutropenia and lymphocytosis developed, neither leucopenia nor anemia resulted from the therapy, as reported in three patients by Volini and

co-workers²⁴ (Fig. 5). Rib bone marrow obtained at operation on the 53rd day of chloramphenicol treatment revealed no evidence of maturation arrest of either erythroid or granulocyte series. Prothrombin levels were normal throughout the period of therapy. In another patient with a branchial cyst, not reported on here, who received 260 gm. of chloramphenicol over a period of 56 days, leucopenia or anemia did not develop.

SUMMARY AND CONCLUSIONS

Chloramphenicol (chloromycetin®) was successfully employed for the treatment of one case of pulmonary actinomycotic empyema caused by *Actinomyces israeli*. This antibiotic administered daily in therapeutic doses over a period of two months caused no appreciable hemopoietic change in two patients.

New York Medical College, Flower and Fifth Avenue Hospitals, New York (Dr. Littman).

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The Ancient Art of Feeling the Pulse.—The *Ars Sphygmica* or ancient science of the pulse dates back into antiquity to long before Galen's time. It is probable that Chinese and Hindu physicians were skilled in feeling the pulse before the dawn of Hippocratic Medicine, and Oriental pulse-lore appears to have developed quite independently of Greek influence. . . . According to legend, Chinese sphygmology was founded by the Emperor Hoamti who is said to have been the author of several books on the pulse about 2500 B. C., and to have been very skilled in the art. . . . The Chinese physician visited his patients in the morning, before taking food, when free from all cares and distractions, and he was enjoined to banish all other thoughts from his mind in order to concentrate on the pulse. This was important because the pulse was timed by the respiration of the physician, four pulsations to each respiration being the natural rate in adults. The patient's arm having been placed on a cushion, the pulse was then palpated at three separate places by the physician's index, ring and middle fingers respectively. . . . At each site, light, moderate, and firm pressure was applied in turn so as to elicit the superficial and deep pulses. All the permutations of these six pulses could not be hastily interpreted, and we may well believe that the whole performance occupied several hours. . . . The art of feeling the pulse was highly developed amongst the ancient Hindu physicians. . . . Susruta (5th century A. D.), the Indian Galen, though most renowned for his surgery, is depicted feeling the pulse. . . . Like the Chinese, the Hindus laid great stress on not only the patient but also the physician being at ease. . . . The pulse was felt at the wrist, on the right side in males and on the left side in females; in the case of eunuchs a nice discretion was necessary in selecting the appropriate side. . . . Before the discovery of the circulation, no rational basis existed for understanding the pulse; it was only possible to describe what the finger felt and to interpret this empirically in terms of the primitive medical ideas of the time.—D. Evan Bedford, *The Ancient Art of Feeling the Pulse*, *British Heart Journal*, October, 1951.

PRIMARY CEREBRAL THROMBOPHLEBITIS

J. Chandler Smith, M.D., Chicago

Thrombophlebitis may be primary or secondary. The latter form occurs in conditions known to be associated with thrombosis of veins such as childbirth, arthritis, infectious diseases, malignant tumors, recent operations, and blood dyscrasias. The primary form is of unknown cause and is often termed recurrent thrombophlebitis or thrombophlebitis migrans. The vessels affected are principally the superficial veins of the upper and lower extremities, although involvement of the visceral veins is not uncommon. Recurrent primary thrombophlebitis of the cerebral veins has been suspected clinically, but a description of the clinical as well as the gross and microscopic changes of such a case has not been recorded in the literature. For this reason the present case is of interest.

REPORT OF A CASE

The patient was a white Jewish man, 52 years, who was well until one week before admission to the hospital, when he noted fatigue and a dull frontal headache. These symptoms persisted, and two days before entering the hospital the patient experienced a generalized convulsion of Jacksonian type, beginning in the left hand, which was followed by a sharp increase in the severity of the headache. Two similar convulsions occurred on the day before hospitalization.

Six years previously the patient had experienced short periods of dizziness that subsided gradually. He was then well until 10 months before admission to the hospital, when short episodes of dizziness recurred. The attacks of vertigo were associated with occipital headache. The patient was hospitalized; physical examination was normal except for symmetrically diminished deep tendon reflexes. The cerebrospinal fluid was normal, and x-rays of the skull were not remarkable. He had been smoking one package of cigarettes daily, and this was stopped. A diagnosis of vasospastic disease of the right side of the cerebrum was made, and the patient was dismissed from the hospital after five days. During the 10 months before his final hospitalization the patient had occasional pain in the lower legs. The pain was brought on by exertion. On several occasions he had a low grade fever that subsided spontaneously.

On admission his temperature was 97.6 F, pulse rate 76, respirations 22, and blood pressure 142/82 mm. Hg. The patient was well nourished and somewhat lethargic and did not appear acutely ill. Results of physical examination of the head, chest, and abdomen were not remarkable. The feet were cold and slightly cyanotic, became dark bluish red when dependent, and blanched quickly on elevation. The dorsalis pedis pulses were absent in both feet. Neurologic examination revealed normal pupillary and conjunctival reflexes. Extraocular movements were normal, the visual fields were not diminished, and results of fundoscopic examination were normal. The function of all cranial nerves was intact. The deep tendon reflexes were markedly diminished in both lower extremities and in the left upper extremity. The superficial reflexes were normal except for a diminished left cremasteric reflex. No pathologic reflexes were elicited. Pain perception was normal. The heel-to-knee and finger-to-nose tests were performed with difficulty on both sides and particularly on the left. Slight weakness and reduced stereognosis were elicited in the left hand. Muscle strength elsewhere was normal.

Urinalysis disclosed no abnormalities. Hematologic examination revealed 13.5 gm. of hemoglobin per 100 cc., 4,310,000 erythrocytes, and 10,000 leukocytes per cubic millimeter, with a

normal differential count and a negative Kahn reaction. Lumbar puncture showed clear spinal fluid and pressure 290 mm. of water; responses to venous compression revealed no subarachnoid block. A sample of fluid was not removed. X-rays of the skull were normal. The electroencephalogram disclosed waves of low frequency with highest amplitudes from the right frontal and right parietal leads. Injection of radioisotopes revealed no focal concentration of the dye. The ventricular fluid was clear, and examination revealed 21 mg. of protein per 100 cc. and no cells. After injection of air into the ventricles, x-rays disclosed nondeviated midline structures with slight depression of the right lateral ventricle with failure to visualize the right posterior horn. These changes were interpreted as suggestive of a right occipital lobe tumor.

The patient became confused, and on the ninth hospital day a flaccid paralysis of the left side developed. Two days later a right parietal craniotomy was performed; a focus of soft bulging cortex, 5 cm. in diameter, was encountered over the posterior parietal region near the vertex. In this region the cerebral veins were thrombosed. A narrow margin of thickened pale yellow adherent arachnoid extended along the side of each thrombosed vein. The arteries were stated to appear unusually small. A similar region of venous thrombosis, 4 cm. in diameter, was present over the midportion of the right frontal lobe. Incision of the soft parietal cortex revealed a subcortical hematoma, 3 cm. in diameter, that was evacuated. The defect was filled with fibrin foam, the bone was not replaced, the dura was left partially open, and the skin incision was closed. The patient appeared in good condition immediately after the operation but died suddenly on the first postoperative day.

AUTOPSY

The brain weighed 1,350 gm. The gyri were flat, and the sulci were narrow over both cerebral hemispheres. Recent subarachnoid hemorrhage was present about an incision in the right posterior parietal region that measured 5 cm. in length. Portions of the veins of the right frontal and both parietal lobes were distended and firm and revealed on each side a narrow margin of pale gray, slightly thickened arachnoid. The surface of the left frontal lobe, both occipital lobes, and the cerebellum, pons, and medulla appeared normal. The arteries of the circle of Willis revealed slight arteriosclerosis. Coronal sections of the cerebrum disclosed a defect in the white matter of the right parietal lobe, measuring 5.5 cm. in diameter, that was filled with gelatine sponge and clotted blood (Fig. 1). This communicated with the surface through the recent incision of the cortex. The cavity lining was shaggy and dark red, and the adjacent white matter disclosed numerous foci of recent hemorrhage. Further coronal sections revealed separate foci of recent hemorrhage, measuring 2 to 20 mm. in diameter, that were present in the right parietal and occipital lobes, the left posterior parietal lobe, and the corpus callosum. A single focus of recent hemorrhage was also present in the midthoracic portion of the spinal cord. The cut surfaces of the midbrain, pons, cerebellum, and medulla were not remarkable. The cerebral ventricles were of usual contour and were lined by smooth, pale gray ependyma.

The heart weighed 375 gm. and was not unusual except for petechiae of the epicardium and a minute focus of dark red discoloration in the wall of the main left coronary artery. There was slight arteriosclerosis of the aorta. An easily detached soft mural thrombus, measuring 1.5 cm. in length, slightly encroached on the lumen of the right common iliac artery. The right and left lungs weighed 375 and 420 gm., respectively, and disclosed slight chronic pulmonary emphysema. The larger bronchi contained scattered plugs of viscid mucus. The liver weighed 2,000 gm. and was not remarkable except for slight chronic passive hyperemia. The kidneys weighed 175 gm. each. The surfaces revealed a diffuse and fine granularity. A bulging red discoloration was present over the surface of the right renal artery and its branches were grossly

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This article has been abbreviated by the omission of Figures 3, 4, and 5. These will appear in the author's reprints.

ing structures, including the paranasal sinuses, were not unusual. The femoral and popliteal vessels were not examined.

Microscopic examination of the left frontal and both parietal lobes of the cerebral cortex revealed large distended veins occluded by recent thrombi (Fig. 2). The vein walls, thrombi, and perivenous arachnoidal spaces were densely infiltrated with polymorphonuclear leukocytes. Old or organizing venous thrombi were not seen in any section. In all other regions the meninges were normal and the vessels were patent. Arteries were distinguished from veins with elastic stains, and the arteries of the brain and meninges were normal except for slight arteriosclerosis in all sections examined. There were many foci of recent hemorrhage throughout the white and gray matter of the cerebrum, and these were frequently ring-shaped about minute central vessels. The cerebral tissue at the margin of the evacuated hematoma revealed focal necrosis, extensive recent hemorrhage and infiltration with mononuclear phagocytes containing blood pigment, and a few polymorphonuclear leukocytes. Sections of the midbrain, pons, cerebellum, and medulla were not remarkable. A single small focus of recent hemorrhage was present in the midthoracic portion of the spinal cord. However, an associated vascular lesion was not identified and the arachnoid vessels of the spinal cord were not remarkable.

Sections of the left main coronary artery revealed slight arteriosclerosis and a minute focus of recent and canalized hemorrhage within the media. Sections of the right common iliac artery revealed a loosely adherent recent mural thrombus. The subjacent arterial wall was infiltrated with lymphocytes, and the vasa vasora were dilated. There was focal necrosis of the right kidney as well as slight arteriolar nephrosclerosis of both kidneys. An occlusion of the right renal artery or its branches was not found. There was moderate reticular hyperplasia of the spleen and slight passive hyperemia of the lungs and liver. Results of microscopic examination of the myocardium, adrenals, prostate, testes, thyroid, pituitary, skin, and skeletal muscle were not remarkable.

The significant anatomic diagnoses included acute thrombophlebitis of the left frontal and the right and left parietal lobes of the cerebrum with recent hemorrhages of the cerebrum and spinal cord. There was slight arteriosclerosis and focal recent and canalized hemorrhage of the left main coronary artery, arteriosclerosis and slight chronic inflammation of the right common iliac artery with recent mural thrombus, and a recent infarct of the right kidney. In addition, the lungs and liver revealed slight chronic passive hyperemia.



Fig. 1.—Coronal section of cerebrum showing recent hemorrhages, site of evacuated hematoma, and thrombosed cerebral vessels at A and B.

Comment.—Examination of the cerebral vessels and brain revealed only recent thrombosis and acute inflammation of the veins. However, the clinical manifestations

of cerebral involvement during the six years before death indicated that the thrombophlebitis was probably recurrent. The cerebral arteries were normal except for slight arteriosclerosis. Lesions of extracranial vessels were found only in the left coronary and right common iliac arteries. The changes of recent and old intramural

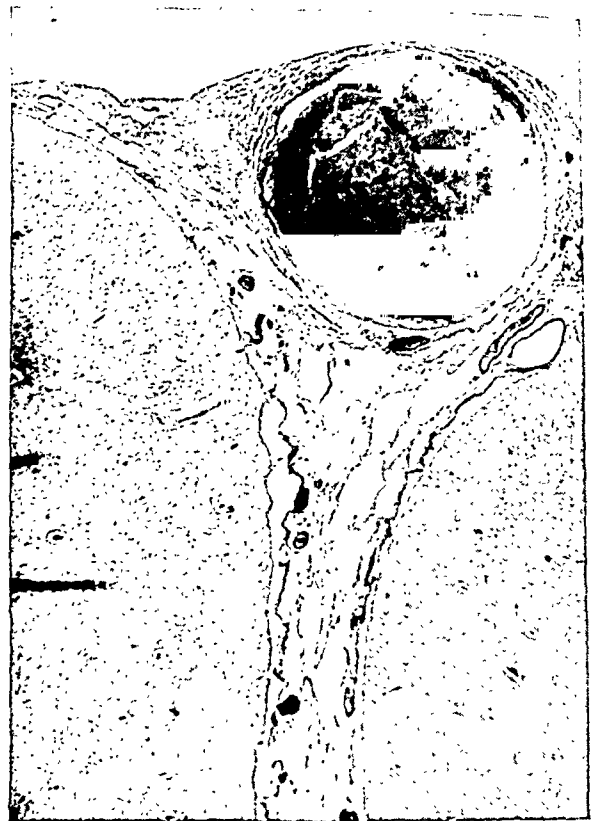


Fig. 2.—Cross section of cerebral vein showing recent thrombus.

hemorrhages of the coronary artery with canalization have been shown by Wartman¹ to be associated with arteriosclerosis. The recent mural thrombus of the right common iliac artery was not organized, and the underlying wall was slightly infiltrated with leukocytes. These changes are related to arteriosclerosis and are not considered to be due to thromboangiitis obliterans. Although autopsy examination revealed no arterial changes consistent with thromboangiitis obliterans, the clinical diagnosis was suggested by the occasional pain in the calves on exertion, the dusky red discoloration of the dependent feet, the blanching of the feet on elevation, and the absence of a palpable dorsalis pedis pulse of both feet.

COMMENT

In 1866 Paget² clearly described the clinical course in two cases of recurrent thrombophlebitis of the extremities of unknown cause. Since that time over 130 case reports of primary thrombophlebitis have appeared in English medical annals. The largest number of cases of this condition was described in 1936 by Barker.³ He reported 79 cases of idiopathic thrombophlebitis of which 40 were recurrent. The latter occurred during middle life, affected males more frequently than females, and did not occur predominately in Jews. The superficial veins of the upper and lower extremities were chiefly affected, and short segments of these vessels became tender, red, firm, and sometimes nodular. The focal thromboses frequently subsided only to recur at another site on the same or opposite extremity, so that

1. Wartman, W. B.: Occlusion of the Coronary Arteries by Hemorrhage into Their Walls, *Am. Heart J.* 15: 459 (April) 1938.

2. Paget, J.: On Gouty and Some Other Forms of Phlebitis, *St. Barth. Hosp. Rep.* 2: 82, 1866.

a migratory character was noted and symmetrical involvement of the extremities was common. The episodes of thrombosis were accompanied by a low grade fever and slight polymorphonuclear leukocytosis. The attacks were recurrent and of varying duration, but the course was self-limited and recovery was ordinarily complete. Barker stated that clinically recognizable arterial lesions did not develop in most cases of idiopathic recurrent thrombophlebitis. The cause remains unknown, although Paget² attributed the condition to a defect of uric acid metabolism, Briggs⁴ to phlebosclerosis, and Herrick⁵ to an unidentified circulating toxin. In an epidemic of thrombophlebitis in East Africa, Manson-Bahr and Charters⁶ emphasized that most of the patients had been given antisyphilitic injections of bismuth and arsenic, although they could not exclude a syringe-transmitted virus as the cause. This group of cases was unique in that most patients also had a stiff neck and relative lymphocytosis. In addition, these cases were sharply localized about two widely separated stations for the treatment of venereal disease. It has been thought that some cases of primary thrombophlebitis represent a venous component of thromboangiitis obliterans. Harkavy⁷ found that, in a control group of 262 smokers, 43 were hypersensitive to intradermal injections of various tobacco extracts. However, in 78 patients with thromboangiitis obliterans, 76 were similarly hypersensitive whereas only two of five patients with thrombophlebitis migrans exhibited hypersensitive reactions. Also, Ackerman and Estes⁸ in following 59 cases of thrombophlebitis migrans for five years reported that discontinuance of the use of tobacco seemed to have little effect in preventing recurrences of thrombophlebitis. Further cases of primary thrombophlebitis of superficial veins were described by Zaus and others.⁹

In other cases there were clinical manifestations indicating involvement of deep as well as superficial veins. These cases were described by Collier and others.¹⁰ The thrombosed deep veins as shown at autopsy included the hepatic, portal, gastric, splenic, gastroepiploic, superior mesenteric, and pulmonary veins as well as the inferior vena cava. In this type of case Barker³ and Ackerman and Estes⁸ emphasized the high frequency of pulmonary infarcts, and in the case of Birnberg and Hansen¹¹ the small intestine became gangrenous.

In several cases of primary thrombophlebitis there were recurrent clinical manifestations that indicated involvement of cerebral veins. These manifestations included convulsions, loss of consciousness, headache, coma, paresthesias, aphasia, and transient pareses. Most of the patients recovered so that anatomic examination of the affected vessels was not performed. However, in 1942 Bucy and Lesemann¹² described a 37-year-old man who had recurrent thromboses of the peripheral veins of four years' duration. He was then well until the age of 52, when periods of unconsciousness, intense frontal headaches, and muscle twitching of one arm developed. Craniotomy was performed, and distended, firm, thrombosed cerebral veins were observed. Tissue was not taken for histologic examination, and the condition gradually subsided. These authors were unable to find a previous description of the pathologic anatomy of a case of primary thrombophlebitis of cerebral veins. In

1947, Davis and Perret¹³ described 11 patients who were thought to have cerebral thromboangiitis obliterans. However, in five of these, (cases 1, 2, 4, 6, and 9) no clinical manifestations of thromboangiitis obliterans of the peripheral vessels were described, and the diagnosis was based on the gross appearance of the cerebral vessels at the time of craniotomy. There was no microscopic examination of the cerebral vessels in these five cases and no statement as to whether the vessels were arteries or veins. It remains unproved that these cases were not examples of primary cerebral thrombophlebitis. Other cases of recurrent thrombophlebitis of peripheral vessels with clinical signs indicating cerebral involvement were reported by Barber and others.¹⁴

It was pointed out by Winiwarter¹⁵ and later by Buerger¹⁶ that thrombosis of superficial veins of the extremities occurs frequently in cases of thromboangiitis obliterans. This was called migratory phlebitis, and Buerger¹⁶ emphasized that in most cases there were absent arterial pulsations or other signs to indicate that the patients had thromboangiitis obliterans. However, in the case of d'Abreu¹⁷ migratory phlebitis preceded the development of thromboangiitis obliterans by 40

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years. Intervals of 20 and 11 years, respectively, were present between the onsets of the two conditions in the cases reported by Ficarra¹⁸ and by Johnson.¹⁹ Signs of cerebral disease during the attacks of phlebitis were not described in these three cases. Although this indicated that the two conditions might be related, Ackerman and Estes⁸ stated that thromboangiitis obliterans developed in only 2 of 59 cases of thrombophlebitis migrans that were followed for over five years.

In a review of the clinical aspects of 500 cases of thromboangiitis obliterans, Hausner and Allen²⁰ found 11 cases in which there were signs indicating disease of the cerebral vessels. Similar cases were also described by Sunder-Plassmann²¹ and by Barron and Linenthal.²² Cases of cerebral thromboangiitis obliterans confirmed at autopsy were reported by Spatz and others.²³ The cerebral veins were specifically mentioned only in the case of Spatz. He stated that occasional vein walls were infiltrated with polymorphonuclear leukocytes and that some small veins contained scattered recent thrombi. However, thrombophlebitis of large cerebral veins or thrombosis of veins apart from inflamed arteries were not described.

SUMMARY

In some instances primary thrombophlebitis precedes or accompanies the development of thromboangiitis obliterans. It is not established that all or most cases of

primary recurrent or migratory thrombophlebitis are associated with thromboangiitis obliterans. Primary thrombophlebitis of cerebral veins occurs in the absence of intracranial arterial disease. The clinical and pathologic features of such a case are described in a patient who had signs suggestive of thromboangiitis obliterans of the lower extremities. So far as can be determined, this constitutes the first record of the clinical course as well as the anatomic examination of such a case.

250 E. Superior St. (11).

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TREATMENT OF CHRONIC PULMONARY TUBERCULOSIS COMPLICATING SILICOSIS

INTERMITTENT POSITIVE PRESSURE BREATHING AND STREPTOMYCIN

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and

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Gaining ascendancy from the writings of Detweiler¹ (1878), rest in bed has become the traditional and essential treatment of pulmonary tuberculosis. However, since the advent of special drugs and procedures, there gradually has developed a regimen with definite indications and limitations for rest, both physical and physiological. It is recognized generally that the supplementary use of streptomycin is required for the acute exudative forms of tuberculosis with toxemia; but, in the chronic types with cavitation and persistent tubercle bacilli in the sputum, artificial pneumothorax, pneumoperitoneum,

thoracoplasty or pulmonary resection may be indicated. There is increasing evidence that sustained rest in cases with emphysema is ineffectual, if not actually disturbing. Similarly, the employment of collapse therapy for atelectasis is harmful, owing to impaired drainage and aeration. Thus, closely associated in treatment are the aspects of a disease for which dynamic therapy as well as rest should be considered.

In an interesting discussion of rest as a therapeutic measure Dock² mentions that the pathology of tuberculosis is usually localized in the apex of the lungs. He suggests that the developments of tuberculosis bear some relationship to the level of the pulmonary arterial pressure and the associated factors of lymph formation, antibody distribution, and toxin elimination. It is noted in a further consideration that tuberculosis is rare in mitral stenosis³ and that a high frequency of the disease occurs in cases of pulmonic stenosis.⁴ The preventive mechanism in the former cases is attributed to the relatively high pulmonic arterial pressure (116 mm. Hg and usually over 40 mm.), while the important factor in pulmonic stenosis supposedly is the bloodless condition of the apex related to lower pulmonic pressure, even during the peak of physical activity.

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4. Auerbach, O., and Stemmerman, M. G.: Development of Pulmonary Tuberculosis in Congenital Heart Disease, *Am. J. M. Sc.* **207**: 219, 1944.

Studies in animals show a development of apical tuberculosis similar to that in man. Medlar and Sasano⁵ observed that the disease in rabbits and cattle occurs typically in the parts of the lung nearest the diaphragm, close to the spine. Surprisingly, the process will shift from the juxtadiaphragmatic region to the apexes after the animals are maintained in the erect position for periods of 11 hours daily. This transposition is ascribed by Dock to the relatively inadequate blood flow farthest away from the heart in the gravitational field.²

In referring to the hypothesis that increased pulmonary arterial pressure may participate in the control of tuberculosis, recent observations suggest that significant variations of pressure should not be anticipated. It is observed, for instance, in normal subjects during exercise that there is no increase of the pulmonary artery pressure and, contrarily, the pulmonary vascular resistance is decreased.⁶ Contrasting are the observations in chronic pulmonary disease indicating that the resting pulmonary arterial pressure may be normal, and in certain instances the elevated pressures at rest may be further increased during exercise.⁶ The observation that acute hypoxia tends to elevate pulmonary arterial pressure⁷ adds complexity to the problem. Thus, it would appear that recumbency in itself is not a specific mechanism for elevating pulmonary arterial pressure. This concept is elaborated with the observation that the pulmonary blood pressure in valvular heart disease is not necessarily limited to the apexes; actually the arterial pressure changes are essentially the same throughout the lung fields.

The quiescence and abeyance of tuberculosis are sometimes attributed to pulmonary fibrosis. Accordingly, the fibrotic process has been regarded as an effective development in the mechanism of healing. While there has been recognition of the potential influence of fibrosis, there is the curious paradox of impaired pulmonary function attributable to destroyed alveoli, bronchioli, and blood vessels, penalizing the useful factors of fibrosis.

With special reference to the mechanism of fibrosis, certain aspects have appeared in recent studies of tuberculosis complicating silicosis: It was disclosed that 97 cases in a group of 750 coal miners admitted to the hospital without selection were affected with tuberculosis.⁸ An interesting feature was the relative high occurrence during the fourth and fifth decades of life, as compared with the higher frequency in the second and third decades of city dwellers unaffected with silicosis. Thus, there is the speculation that silica or the fibrosis is a predisposing cause of tuberculosis, with a supplementary influence of retardation as induced by the fibrous tissue. An additional aspect of the study relating to the course following the onset of manifest tuberculosis indicated that longevity was two to three years among those treated at home. In contrast was the experience at the White Haven Sanatorium, where certain coal miners undergoing systematic care lived 5 to 10 years or more, suggesting that medical care in itself was more valuable than the factor of fibrosis. Indeed, the issues of fibrosis appear complex and variable.

In recent years, the role of segmental and lobular physiology in the development and perpetuation of chronic pulmonary diseases has aroused considerable interest. The basic aspects relate to ventilation alveolar tension, and the unique mechanism of capillary blood drift and intra-alveolar air drift, as discussed by Churchill.⁹ It is mentioned that a minor pulmonary embolism will disclose a collateral drift in the pulmonary capillary network of sufficient magnitude to maintain a slowly moving circulation, despite occlusion of the sizeable terminals of the pulmonary artery. This is illustrated in cases with increased back pressure in the pulmonary veins or abnormal slowing of the capillary stream by reduced respiratory excursion when a bland infarct may be converted into a hemorrhagic infarct. Churchill⁹ suggests that this capillary blood drift crosses the segmental boundaries of the lung. With the collateral air drift there also are the features of a compensatory mechanism or an emergency device of respiration. The sequence of events relates to the trapping of air in the alveoli by obstruction to its outflow and the effects of cough, characteristic of pneumonia or paroxysmal asthma, as follows: (1) inspiratory widening of the terminal bronchioles; (2) early in expiration the quick closure of the laryngeal sphincter with elevation of the endobronchial air tension by the muscular effort of a cough or grunt; (3) trapping of air in lobules under increased tension; and (4) slow reduction in the tension by collateral air drift through the pores so that in the next cough the lobule receives a blast of fresh air with renewed oxygen supply. The importance of the collateral air drift of the lungs was emphasized in World War II, when aspiration of blood and secretions from the pleura and air passages, and the employment of intercostal nerve block replaced the earlier practice of using morphine and tight strapping of the chest, resulting in a remarkable reduction of post-operative edema. While the blood drift may be less important than air drift as a compensatory mechanism of respiration, since the blood has already passed through functioning alveoli with resultant oxygenation, there is the influence of blood in maintaining the integrity of capillary walls.

The normal mechanism of chronic pulmonary conditions relates to the preservation of the whole dynamic action of the respiratory system with its adequate ventilation and active capillary circulation. This involves the elaborate neuromuscular structure surrounding the air passages and the constant and vigorous activity of the bronchus. Of special interest is the inspiratory dilatation and lengthening of the bronchi, and constriction with shortening during the expiratory phase.¹⁰ It is apparent that integration of pulmonary ventilation and alveolar

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9. Churchill, E. D.: The Segmental and Lobular Physiology and Pathology of the Lung, *J. Thoracic Surg.* 18: 279, 1949.

10. Macklin, C. C.: The Musculature of the Bronchi and Lungs, *Physiol. Rev.* 9: 1, 1929.

air tension, with preservation of the bronchiole and respiratory bronchiole at the site of the sphincters surrounding the necks of the air sacs, is an important prerequisite for normal function.

With reference to the minute processes of the respiratory system, the secreting membrane of the segmental bronchus introduces a peculiar factor of obstruction to the air passages that may not occur at the bronchiolar level. As a consequence, blockage of the segmental bronchus and retrograde filling or drowning of the bronchioles and air sacs will result.¹¹ However, as Churchill⁹ observed in two children with the so-called Kartagener syndrome, the developments were relatively benign in the absence of infection. This absence of pus was attributed by him to the timely use of antibiotics and re-expansion of the pulmonary segments. In another case of Kartagener syndrome, bronchiectasis followed an attack of acute bronchitis.⁹ From these interesting considerations, it appears that the combined influences of impaired ventilation elaborated in the disturbances of abnormal air drift and blood drift pose important prob-



Fig. 1.—H. B., male, 52, with the diagnosis of fibroid type tuberculosis (apical) of both lungs with tubercle bacilli in the sputum and the manifestations of marked pulmonary emphysema. A (Nov. 29, 1949), obtained before treatment with intermittent positive pressure breathing. B (Oct. 12, 1950), taken after six months' treatment; symptomatic improvement with reduction in the areas of increased density were attributed to improved bronchiolar drainage and alveolar aeration.

lems in the treatment of most cases of chronic pulmonary disease, fibroid tuberculosis with emphysema being no exception.

In the physiological disturbances of emphysema per se, there is a faulty distribution of air in the lungs. This impairment of function is attributed to mixing and dilution difficulties with unequal alveolar aeration and perfusion caused by the loss of pulmonary elasticity and obstructive changes in the bronchioles, accentuated by inspissated mucus, fibrous contraction, or bronchospasm. Inadequate distribution of inspired air lowers the alveolar oxygen partial pressure (pO_2) and the percentage saturation of arterial blood oxygen due to the elevated mean pO_2 gradient between the alveoli and the arterial blood. In some cases the increased mean gradi-

ent of pressure for oxygen between the alveoli and arterial blood approaches 50 mm. Hg (normal, 5 mm. Hg), and the average resting arterial oxygen saturation is moderately reduced but poorly correlated with pulmonary function impairment.¹¹ It is interesting that the arterial oxygen saturation values obtained during mild exercise may reveal significant differences with respect to disability and the degree of emphysema, as compared with the resting level.

Fatigue, an important influence in disability, reflects the results of physical effort, lack of proper rest, and disturbed pulmonary function. This is notable in silicotic coal miners plagued with paroxysmal racking cough and dyspnea. In the progressive cases, rest in bed is possible only while the patient is lying with the back supported on two or more pillows; with advanced disease the patient can obtain rest only in a reclining type of chair or in straight chair, while leaning forward with the arms hanging down or supported on a window sill or table. Other factors participating in the phenomenon of fatigue are restricted exercise and the occurrence of acute chest colds involving the bronchioles.¹² There are both the innate and direct disturbances of the structural disease with the concomitant factors of a vicious circle. For example, with enforced rest there is impaired pulmonary ventilation, and with insufficient rest the ramifications of lowered resistance are brought into play.

The treatment of uncomplicated silicosis relates to (1) symptomatic relief for dyspnea and choking cough; (2) measures that favor the drainage of "free silica" and abnormal secretions of the bronchioles; and (3) improvement of respiratory function with dynamic therapy.¹³ It has appeared that therapeutic rest in bed is contraindicated, since the important requirements are for the acceleration of bronchial drainage and restored alveolar aeration. The use of respiratory exercise as obtained with intermittent positive pressure breathing treatments provides a midway course in favoring pulmonary function without the handicaps of overexertion.¹³ A pertinent question has occurred with the discovery of tuberculosis during the course of the treatments (four cases): Is intermittent positive pressure breathing therapy indicated or contraindicated in tuberculosis? Indeed, there has been a dilemma when symptomatic relief from the silicosis occurred in the shadow of the possible aggravation of tuberculosis. While recalling the unsatisfactory results from the accepted treatment of tuberculosis in this type of patient, our interest turned guardedly to the use of intermittent positive pressure breathing.

The present observations are based on the study of 18 cases of tuberculosis with extensive fibrosis, emphysema, tubercle bacilli in the sputum, and the symptoms of dyspnea, weakness, racking or choking cough, and difficult expectoration. It is emphasized that these patients were classified as "old chronics" with limited manifestations of active tuberculosis, the chief disturbance being physiological as related to the associated pulmonary conditions. Actually, the diagnosis was established only with the discovery of tubercle bacilli in the sputum and the presence in the x-rays of localized apical densities with or without cavitation and deviated trachea. A series

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12. Gordon, B., and others: Considerations of the Clinical and Physiologic Factors in the Treatment of Chronic Pulmonary Conditions, *Dis. Chest* 19: 271, 1951.

13. Gordon and others,¹² Motley, H. L.; Lang, L. P., and Gordon, B.: Use of Intermittent Positive Pressure Breathing Combined with Nebulization in Pulmonary Disease, *Am. J. Med.* 5: 853, 1948.

of six additional cases of arrested or suspected tuberculosis, nonsilicotic in type, are included, since the manifestations and basic problems simulated silicosis with complicating tuberculosis. It was observed that previous treatment with enforced rest in the recumbent position had been generally ineffectual because of the respiratory symptoms, and artificial pneumothorax and thoracoplasty were contraindicated. Continuous immobilization of the lungs by residence in an equalizing chamber,¹⁴ a method advocated for treatment in certain cases of tuberculosis with cavitation and acute disease, was deferred (Fig. 1), because it appeared that this form of pulmonary restriction favored the retention of secretions and consequent dyspnea. With reference to drug administration, it had been noted repeatedly that narcotic preparations reduced cough but coincidentally lessened expectoration, accentuating the difficulties of reduced pulmonary aeration. The action of bronchodilator drugs given by aerosol was disappointing.

In the physical examinations, the occurrence of dyspnea, cough, expectoration, elevated temperature, accelerated pulse rate, and rales, and the presence of tubercle bacilli in the sputum were tabulated before, and after the course of treatments for indications of improvement or aggravation. Roentgenograms of the chest also were obtained before and during the treatments and one, two, three, or six months later.

The regimen of intermittent positive pressure breathing treatments,¹⁵ consisting of 100% oxygen and racemic epinephrine solution (vaponefrin,[®] 8 drops diluted in an equal amount of isotonic sodium chloride solution) was employed for periods of 5 to 15 minutes, once or twice daily, with discontinuance for three or four days when there was relative freedom from disturbing pulmonary symptoms.¹⁶ The maximum period of treatment was three months, except in two patients, who had received the treatments, with interruptions, for more than one year. Of the entire series, nine were hospitalized continuously; others were treated alternately in the hospital and at home. Streptomycin, 1 gm. daily, was given parenterally (simultaneously) in five patients with a high number of tubercle bacilli in the sputum. All patients followed their customary habits of sleeping and resting, which were variable, owing to the dyspnea.

The following data were noted: A constant feature was the reduction of dyspnea and choking cough with increased expectoration, initially, followed by reduction of the sputum, the improvement being characteristic in coal miners with uncomplicated silicosis. With lessened dyspnea there was the expressed desire to rest in bed, often in the recumbent position. Improved appetite, a sense of well-being, and a gain of 2 to 4 lb. (1 to 2 kg.) occurred in nine cases. The increase of tubercle bacilli, followed successively by a decrease, was an interesting feature in three cases. In one instance the sputum displayed transiently a variety of colors and tenaciousness. The physical signs, including alterations in the percussion note, rales, and exaggerated breath sounds, were not permanently influenced. It was striking, however, that after each treatment there usually was a transient reduction of musical rales, sometimes associated with louder breath sounds and freer movements of the chest. These alterations, found also in uncomplicated silicosis

treated with intermittent positive pressure breathing, were attributed chiefly to increased bronchiolar drainage and alveolar aeration, rather than to specific effects on structural disease. In the x-rays there were no appreciable changes in the type or distribution of the shadows, except in two cases in which there were large radiolucent bodies in the areas formerly occupied by dense shadows and two cases with suggestive extension of the tuberculosis; in two cases there was striking regression (Fig. 2). It is interesting that the appearance of the radiolucent structures was coincidental with marked expectoration and the increased number of tubercle bacilli in the sputum. One patient died in the third week of treatment, during an acute episode of intercurrent infection with a possible extension of the tuberculosis; two died approximately six months after the treatments were terminated. Therapy was discontinued in two instances because of persistent elevation of temperature and weakness, with

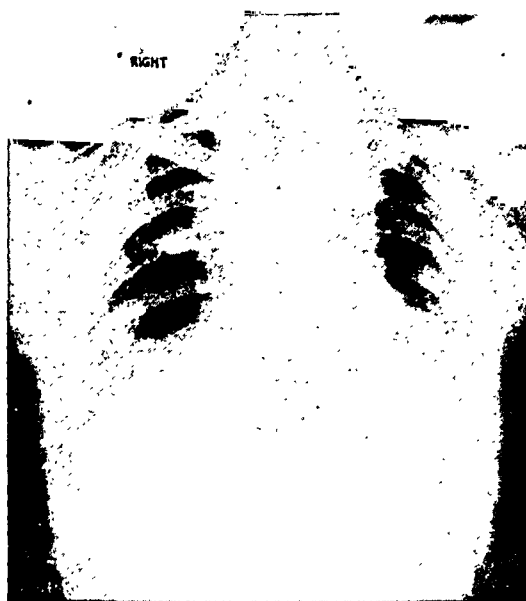


Fig. 2.—Male, age 31, with fibroid pulmonary tuberculosis (apical and basal) and marked emphysema. Marked dyspnea with difficult expectoration followed a period of prolonged rest in bed and residence in an immobilizing chamber; intermittent positive pressure breathing treatments reduced the dyspnea and facilitated expectoration.

a suggestive spread of the tuberculosis. It is of interest that seven patients requested a resumption of the treatments, previously discontinued for clinical evaluation. These requests were based on the increasing dyspnea and the inability to expectorate effectively.

The present use of intermittent positive pressure breathing treatments in tuberculosis was undertaken primarily as a means to determine the effects of bronchiolar and alveolar dilatation and improved pulmonary drainage on the immediate and subsequent course of the disease, with special reference to symptomatic improvement and the ability of the patient to rest more adequately in

14. Barach, A. L.: Continuous Arrest of Lung Movement; the Treatment of Pulmonary Tuberculosis in an Equalizing Alternating Pressure Chamber, *Am. Rev. Tuberc.* 43: 56, 1941.

15. The apparatus is manufactured by V. Ray Bennett, 8154 Beverly Blvd., Los Angeles, and The Mines Safety Appliances Company, Pittsburgh.

16. The usual periods of treatment with intermittent positive breathing are 20 minutes, two or three times daily for several weeks or months; the reduced periods in the present tuberculous cases were preferred in order to avoid possible fatigue.

the recumbent position. The rationale was based chiefly on the concept that maximum rest ordinarily indicated for tuberculosis was impossible, because of dyspnea, choking cough, difficult expectoration, and their fatiguing and traumatizing influences. It had been recognized that abnormal bronchiolar and alveolar secretions interfered with the mechanism of alveolar aeration and perfusion, favoring the development of new disease and the concomitant functional disturbances. In the over-all consideration, the tuberculous infection per se appeared less disturbing than the vagaries of physiologic dysfunction. The findings emphasize that symptomatic relief from dyspnea and difficult expectoration occurred with about the same constancy as would be expected in uncomplicated silicosis.

There has been speculation as to the possibility that increased activity of the tubercle bacilli occurs under the influences of 100% oxygenation, as introduced under intermittent positive pressure breathing. The question is pertinent, since the report of Rich and Follis¹⁷ indicated that the growth of tubercle bacilli experimentally may be influenced by increased oxygen tension. There are no data in the present study suggesting that increased oxygenation in itself caused untoward effects. Indeed, it would appear that the immediate action of oxygen bacteriologically, if any, was transient, since the treatments were of short duration. More important, perhaps, is the concept that, with improved aeration of the alveoli, the advantages of symptomatic relief would outstrip the theoretical hazard of new activity of tuberculosis organisms. The question that trauma to the lungs may result from the increased pressure of oxygen with forced inspiration has also been raised. It should be noted in this connection that the oxygen flows according to the patient's own pattern of breathing, the maximum peak inspiratory pressure being equivalent only to 20 cm. of water, a distinctly lower pressure than would occur even in minor cough (maximum pulmonary pressure during cough varies from 40 to 100 cm. of water, or more), and the pressure becomes atmospheric during expiration. As the lungs are filled with oxygen under the mechanism of intermittent positive pressure breathing, the rate of flow is approximately one-half the flow rate during the initial phase of expiration. Actually, the flow of expiration exceeds the force of inspiration, owing to the rapid drop of pressure during expiration. With this mechanism, the passage of mucus down the bronchial system during inspiration is minimal, as compared with the flow rate that favors an upward movement of mucus. In a sense, the phenomenon of expiration simulates the mechanism of cough in a very reduced manner. With reference to the efficiency of cough, it should be emphasized that the mechanism operates effectively only when air is present in the alveoli. This is elucidated in acute atelectasis, when the pathological and physiological conditions deprive air from the affected region and prohibit the expulsion of contents. In such conditions treated with the combination of helium, 30% or 40%, and oxygen, 60% or 70%, introduced under intermittent positive pressure breathing therapy for periods of 20 minutes every four hours, remarkable expansion of the lung is sometimes noted.

Admittedly, the paradox of employing intermittent positive pressure in silicosis with complicating tuberculosis is not easily composed, in light of the value and indications for rest as a therapeutic measure. As mentioned previously, the indications are weighed in the balance between respiratory quietude and increased alveolar aeration that may be harmful or valuable, respectively. It should be re-emphasized that the accomplishments of intermittent positive pressure breathing in chronic pulmonary tuberculosis are not curative. The procedure is used primarily in the channel of symptomatic relief in order to obtain ultimately the resultant benefits of adequate pulmonary function, as indicated in pulmonary emphysema and inoperable bronchiectasis.¹²

SUMMARY AND CONCLUSIONS

1. The present study, dealing with chronic pulmonary tuberculosis associated with anthracosilicosis, indicates that the physiological disturbances of emphysema and fibrosis are basic causes of dyspnea, racking or hacking cough, and difficult expectoration.
2. Rest in bed with so-called collapse therapy, the accepted treatment in pulmonary tuberculosis, is not always applicable, since respiratory quietude sometimes accentuates the disturbances of emphysema and fibrosis of the lungs.
3. Intermittent positive pressure breathing treatments with aerosols of bronchodilator drugs have been employed guardedly in a selected group of chronic pulmonary tuberculosis with emphysema and fibrosis; streptomycin was administered as supplementary treatment in cases with suspected acute exacerbations of the disease.
4. The relief of manifestations, as noted in the majority of the cases, was attributed to improved pulmonary drainage and alveolar aeration.
5. The symptoms and function disturbances of emphysema and fibrosis of the lungs associated with pulmonary tuberculosis pose the fundamental need for physiological adjustment, without which the normal processes of healing may be retarded.
6. The aspects relating to the development and dissemination of pulmonary tuberculosis are reviewed.

17. Rich, A. R., and Follis, R. H., Jr.: Effect of Low Oxygen Tension upon the Development of Experimental Tuberculosis, *Bull. Johns Hopkins Hosp.* 71: 345, 1942; abstracted, *Tr. A. Am. Physicians* 57: 271, 1942.

Peptic Ulcer in Children.—It is apparent that peptic ulcer does occur frequently in children and that its likelihood must always be considered whenever persistent gastrointestinal disturbance occurs. The peptic ulcers of childhood are usually acute in type during infancy. The onset of symptoms is often precipitous and without recognizable premonitory symptoms or signs. The majority of the lesions in this age group either bleed profusely or perforate. As the age of the child increases, the type of ulcer increases in chronicity. The incidence of bleeding and perforation diminishes and the likelihood of pyloric stenosis and scarring of the duodenum becomes greater. The probability of persistent abdominal pain, frequently of the adult type, also increases. The prevalence of peptic ulcer in children is somewhat greater in the male than in the female (approximately by a 3 to 2 ratio in all age groups). Also, duodenal lesions occur more frequently than gastric.—Russell H. Morgan, M.D., *Peptic Ulcer in Children, The American Journal of the Medical Sciences*, November, 1951.

MEDICAL IDENTIFICATION IN THE "NORONIC" DISASTER

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and

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The identification of large numbers of mutilated bodies may be among the many difficult problems to be faced in major disasters resulting from fire or explosion. Such was certainly the case when the steamship "Noronic" was gutted, while tied up at the pier in Toronto, Canada, on Sept. 17, 1949. The deaths of 119 persons were directly attributable to the disaster, and the bodies of 107 were burned beyond possible recognition. The task was undertaken by a Medical Identification Committee, composed of pathologists, radiologists, and dentists.¹ This group succeeded in identifying 116 of the 119, and the results have never been equalled. In these uneasy times, when extensive preparations against disaster are being made, the experiences and achievements of such a medical study deserve a place in the records.

The identification of burned bodies is not a new problem, and it has been met on a large scale in several recent fire disasters. Four hundred ninety-one persons lost their lives in the fire at the Cocoanut Grove in Boston in 1942.² Plans laid during World War II in the Disaster Preparedness Program of the Boston Area encompassed such an eventuality, and almost all the bodies were identified within a few days. The majority of the deaths resulted from suffocation, and most of these bodies were not badly disfigured. Jewellery, clothing, wallets, and keys on the bodies, as well as facial features, were preserved and were easily recognized by relatives and friends. The attending physicians were fully occupied with the care of many persons with serious burns and, apparently, played no part in the identification of the dead. In the Texas City explosion³ in 1947, between 500 and 600 were killed. All but 61 mutilated bodies were identified by the Texas State Safety Council. The medical services were taxed to the limit in attending more than 3,000 casualties and were not involved in the identification plan. Autopsy was performed on only a few bodies. In both the Hartford circus tent fire and the more recent explosion at South Amboy, N. J., the identification work was left to the police. Indeed, identification in general has become a special branch of scientific police procedure. Fingerprinting, which has proved to be the most accurate method, is the basic technique in identification, but several others are employed. Dental examination may be used when the body is decomposed or mutilated, but very seldom is anatomical evidence necessary.

In the "Noronic" disaster the devastation wrought to such a large number of bodies put the possibility of identifying many of the victims beyond the limitations of the usual techniques of identification. One hundred and eleven charred bodies were recovered from the ashes and twisted wreckage of the ship, and all but four of these were burned beyond recognition. Five other persons were drowned in the harbor beside the ship, and one woman was dead on arrival at the hospital from injuries received while escaping the fire. Although a number of survivors

were treated for minor burns in the emergency wards of the hospitals, relatively few persons with serious burns were found, and only two women died in the hospital some weeks after the fire. The bright red blood of the body in most of the burn victims suggested that carbon monoxide poisoning caused death, rather than the burns, but it was thought that little could be gained in attempting to prove this point under the circumstances of this catastrophe. The major problem in the "Noronic" disaster was identification of the dead.

A general résumé of the extent of the burns gives some understanding of the difficulty of the situation. In 49 bodies every square inch of skin and subcutaneous tissue was burned away, and all the underlying muscles were charred. In only 20 bodies was there sufficient skin remaining on the fingers to enable the taking of fingerprints. In 86 bodies the calvarium was burned open, in 73 both sides of the thoracic cage were destroyed, and in 85 the abdominal wall was demolished. In only 16 cases did all four extremities remain intact, although charred, and in 22 cases all four extremities were absent. Those limbs, or parts of limbs that remained, often consisted only of cracked fragments of bone held together by blackened muscle. This limited the possibility of using such calculations as Pearson's formulas for the estimation of height. The bodies were made rigid by the burns, and the joints were frequently burned open.

Besides the damage to the bodies, there were other difficulties to be met. What property remained on the bodies was badly destroyed. There was nothing to indicate the site on the ship where each body had been found. When it came to determining who was lost in the fire, the disaster relief teams found themselves in a predicament. There was, at first, no passenger list for the ship, and this, combined with the failure of some survivors to report their escape, increased the lists of the missing. Then, none of the casualties were known to local residents, because all of the ship's passengers were tourists, the majority of whom came from Cleveland, Detroit, and surrounding communities. The relatives and friends of the missing, were, also, in strange surroundings when they came to Toronto, and this, together with their anxieties, added further to the confusion.

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This project was conducted under the direction of the Honorable Dana M. Porter, Attorney-General of the Province of Ontario, and Hiram E. McCallum, Mayor of the City of Toronto. The City of Toronto and the Province of Ontario shared in the entire cost of the investigation.

1. The members of the Medical Identification Committee for the "Noronic" disaster were Dr. W. L. Robinson (Chairman); Drs. A. C. Singleton, E. A. Grant, T. C. Brown, R. J. Delaney, W. Anderson, J. Simpson, F. Bryans, G. Cates, H. Cleland, and D. Wilson.

2. Aub, J. C.: Management of the Cocoanut Grove Burns at the Massachusetts General Hospital, Philadelphia, J. B. Lippincott Co., 1943.

3. Blocker, V., and Blocker, T. G.: The Texas City Disaster; Survey of 3,000 Casualties, *Am. J. Surg.* 78: 756, 1949. Identification in Disaster: Texas Department of Public Service, 1948.

It was necessary, for several reasons, to identify those who died in the fire, but the first consideration was the personal feelings of the relatives and friends, who could never rest until the deaths of their lost ones could be established beyond doubt. On the other hand, the fire created a wide range of mundane problems, of which a swift resolution was of equal import to those grieving persons. There were wills to be probated and estates to be settled. Insurance payments and claims awaited the issuance of death certificates, and premium payments had to be continued until this was forthcoming. Business associations, partnerships, and other arrangements were dislocated. There was the question of remarriage of survivors. In addition, it was important to forestall fraudulent attempts to collect insurance and false claims of death, and to guard against the desire of some persons to disappear. Therefore, there was every justification for embarking on an attempt to identify the victims.

TABLE 1.—Lesion or Condition Discovered at Autopsy and Used in Identification

Organ		Lesion or Condition	Cause Incidence
Appendix		Perforation (old)	1
Bones	Spine	Scoliosis	1
		Kyphosis	2
		Osteoarthritis	7
		Osteoarthritis	1
	Knees	Osteoarthritis	1
	Os calcis	Osteoarthritis	1
	Mandible	Atrophy	1
Kidney		Polycystic (bilateral)	1
		Pyelonephritis, chronic	1
		Hydronephrosis	1
Lung		Calcareous degeneration (apical)	1
		Collapse (pneumothorax)	1
		Bronchiectasis	1
		Tuberculosis (treated)	2
Ovary		Corpus luteum	1
		Cyst, follicular	1
		Graafian follicles	1
		Atrophy	1
Pericardium		Pericarditis (fibrous)	1
Peritoneum		Adhesions	1
		Hernia	3
Pleura		(Adhesions) Fibrous pleurisy	2
Skin		Pilonidal sinus	1
Uterus	Cervix Body	Nulliparous	1
		Premenstrual endometrium	1
		Menstruation	2
		Atrophy	1
		Prolapse	1
		Leiomyoma	2

Against the mutilation of the bodies in the “Noronic” disaster all the recognized techniques of identification had to be employed. They were modified to suit the special circumstances, and new ones were developed. A significant advantage was gained when it was proved that the number of persons missing in the fire tallied exactly with the number of bodies in the mortuary. The Red Cross had been able to compile an accurate passenger list by tracing every survivor and eliminating all but the “Noronic” victims from among the general missing persons’ lists. Consequently, the proposition developed into a comparison of bodies with missing persons, and the study divided itself into two parallel investigations—the examination of the bodies, and the search for information on the missing persons. Both phases of the investigation were conducted simultaneously and by the same personnel. The former will be considered first.

The examination of the bodies included an autopsy, a dental study, x-ray examinations, fingerprinting, and a thorough description of all property and valuables on the body. Where indicated, special anatomic and chemical

studies were done. The pathologists, radiologists, and dentists were aided, when necessary, by such specialists as were needed from the staffs of the University of Toronto, the Toronto General Hospital, and the City Department of Health. Working in conjunction with these men were the Toronto police force, who attended to the identification and protection of property on the bodies, the Federal Bureau of Investigation, who did the fingerprint studies, and the Canadian and American Red Cross, who conducted the social service work and maintained teletype communication between Toronto and the cities and towns all across the United States that could supply information about the victims. All these examinations took place at about the same time, and each will be dealt with in turn.

The autopsies were begun the day after the fire, and only an initial general examination of each body was completed on that day. As the bony structures could not be disturbed until the roentgenograms were made particular attention was paid at this stage to listing the damage from burns on the bodies. When the roentgenograms were completed the autopsies were carried further and special care was taken to preserve the tissue, so that none of the evidence would be destroyed. The viscera were, insofar as was practical, sectioned in situ. The signs of old injuries and operations were sought especially, as were developmental abnormalities. The internal organs were found badly charred whenever the abdominal and thoracic walls had been destroyed. The live lungs, and spleen were usually shrunken and dried, and the heart was hardened. The brain was almost always putty-like mass, whether or not the calvarium was intact. The kidneys and pelvic viscera were usually preserved as were the intestines, except for exposed loops, which were burned away. The adrenals and pancreas were always intact. Where indicated, sections for microscopic study were taken. Decomposition of the bodies was never a serious problem, because they were charred and because they were stored in an unheated building. The soft tissue that remained was protected by keeping the bodies in metal sealers with carbon dioxide ice and formaldehyde (“formalin”)-soaked rags.

Despite the destruction of the bodies, the autopsies revealed a wide variety of lesions. Among those that were of value in identification were osteoarthritis of the spine in seven instances, inguinal hernia in three, and in two cases each kyphosis, pulmonary tuberculosis, pleural effusion, leiomyoma of the uterus, and menstruating endometrium. Table 1 lists these, together with those that played a part in single cases. Congenital abnormalities of the skeleton were found in two cases and, each, formed part of the evidence. These deformities were spina bifida and an android pelvis. Signs of old injuries were found in only a few cases, but, again, they were useful in identification. There were two cases in which the eyes had been destroyed. There was one case in which the scar of an old penetrating injury of the anterior abdominal wall was found. In only two cases were old fractures discovered, one in the left metatarsal and the other in the left ankle. A wedge-shaped deformity of the second and third lumbar vertebral bodies was also included in this group. The manifestations of previous surgical procedures were a common finding and entered

oftenest into the identifications. In 18 bodies an appendectomy had been done, and in 9 of these this evidence was a necessary item in their recognition. Similarly, four bodies were recognized partially through an old cholecystectomy; three others showed this operation, but this information was not used. Table 2 lists the congenital abnormalities, old operations, and previous injuries, together with their incidence as a factor in identification. Many other lesions were found but are not listed here, because they were not made use of in this project and, still more, were never included in the autopsy records because the exigencies of the disaster prevented the examination of a body beyond what was necessary to establish its identity.

The dentists examined 87 of the bodies. Twelve bodies had been identified before dental studies were made, and in 19 more the jaws and mouth had been destroyed by fire. When necessary, dentitions were reexamined, an x-ray examination made, and the dentures submitted to specialists from manufacturing laboratories. The details of the dental investigation are to be published by Dr. E. A. Grant.⁴ As with other phases of the plan, destruction of the jaws and teeth obscured the full details of the dentitions, and several types of dentures were hopelessly distorted or even disintegrated by the heat.

The fingerprint examinations were also difficult to make, and, in the bodies in which sufficient skin did remain, the ordinary methods of obtaining the finger ridge patterns could not be used. The fingers were therefore sent to the F. B. I. in Washington, where the skin was cut from their palmar surfaces. After softening, the sheets of skin were pressed between glass plates, so that the patterns could be photographed. The homes of the missing persons were searched for their fingerprints, and the patterns sent for comparison. In no cases, however, did this bring to light any valuable evidence.

The postmortem of the bodies by x-ray was an entirely new project. In 1926 Culbert and Law⁵ reported the identification of a body by roentgenographic means, 216 days after the disappearance of the person, and, in 1944, Dutra⁶ described the identification of a body burned beyond recognition in an automobile, but, apart, from these two cases, such a study had not been reported. Seventy-nine bodies were examined in the "Noronic" investigation. Insofar as possible the views made duplicated those used in clinical roentgenology, but the brittle state of the bodies, and the deformity and stiffening produced by the burns, made this difficult, and the films were clouded by metallic and amorphous foreign bodies, which obscured the bony outlines to some extent. The serous surfaces were flecked by sand, ashes, and embalmers' hardening compound, and melted and chipped paint was embedded in soft tissue. When the bodies had been washed out, the bony structure was cleared considerably. In all, 1,020 films were used, amounting to an average of 13 per person.

A thorough search of the ship's wreckage brought forth much evidence of adjuvant value to the investigators. Correlation of the sites where fragmentary human remains and personal property were found, with the ship's deck plan and the steward's lists of cabin allocations, gave corroborative evidence in several cases and

sometimes provided the key to the solution of an identification.

From the reports of all the different examinations of each body a dossier was made, and care was taken to add to it additional evidence, correspondence, or notes pertaining to that body. To use in identification such a mass of information on more than 100 bodies the data had to be classified. This was begun after the initial examinations of the bodies had been completed and was amplified as more information was obtained. The bodies were categorized in accord with their features in common, and old operations, height, weight, age, dental characteristics, and property were prominent groupings. This system facilitated the search for bodies that might answer the description of some missing person.

The analogous side of the identification was the collection of information about the missing persons. This required a prolonged investigation, which was, as has been

TABLE 2.—Identification Value of Abnormalities Found in Victims

	Total Cases	Abnormality Valuable in Identification, No. of Cases
Congenital Abnormalities		
Spina bifida	1	1
Android pelvis	1	1
Operations		
Appendectomy	18	0
Circumcision	6	1
Cholecystectomy	7	4
Bronchogram	1	1
Enucleation	2	2
Herniorrhaphy	1	1
Hysterectomy		
Total	4	4
Subtotal	1	1
Ligation of fallopian tubes	1	1
Mastoidectomy	1	1
Pneumothorax	1	1
Oophorectomy	3	2
Sinusotomy (pilonidal)	1	1
Thyroidectomy	2	1
Previous Injuries		
Fractures		
1st metatarsal	1	1
Left ankle	1	1
Laceration of the anterior abdominal wall (R. L. Q.) (motorcycle accident) ..	1	1
Perforation of orbit oculi	2	2
Deformity (wedge shape) L ₂ and L ₃	1	1

mentioned previously, parallel to the autopsies. At the outset, any person seeking someone lost in the fire was interviewed by a social service worker who recorded a general description of the missing person, his address and those of his relatives and business associates, and such general information as might be useful. The next step was to examine the property recovered from the ship and the valuables held by the police. When this had been done, the relative was brought, with the form filled out by the social worker, to the pathologists and the dentists, who used this form as the basis for opening their files on a particular missing person. Relatives were frequently asked about serious illnesses, injuries, operations, and deformities suffered by the missing person, with the approximate dates of occurrence and the names of the hospitals and medical and dental attendants. Sometimes the characteristics of a missing person were so striking that

4. Grant, E. A.: Ontario Dental Journal, to be published.
5. Culbert, W. L., and Law, F. M.: Identification of a Body by Comparison of Roentgenograms of the Nasal Accessory Sinuses and Mastoid Processes, J. A. M. A. 88: 1634 (May 21) 1927.
6. Dutra, F. R.: Identification of Person and Determination of Cause of Death from Skeletal Remains, Arch. Path. 38: 339, 1944.

of atrophy was consistent with the history of old traumatic injury.

Four months after the fire the committee was left with three unidentified bodies and three unidentified missing persons. The files on all the cases contained a great deal of information, and, although it was not improbable that the three bodies were those of the three missing persons, there was not enough positive evidence. In these cases failure had to be conceded. The identification of the "Noronic" victims was therefore closed.

Before the files were closed on the "Noronic" disaster, the committee undertook a comparative review of the methods employed in identifying these badly burned bodies. Consideration of the relative value in the entire identification project of the different types of investigation substantiated the general impression that the results

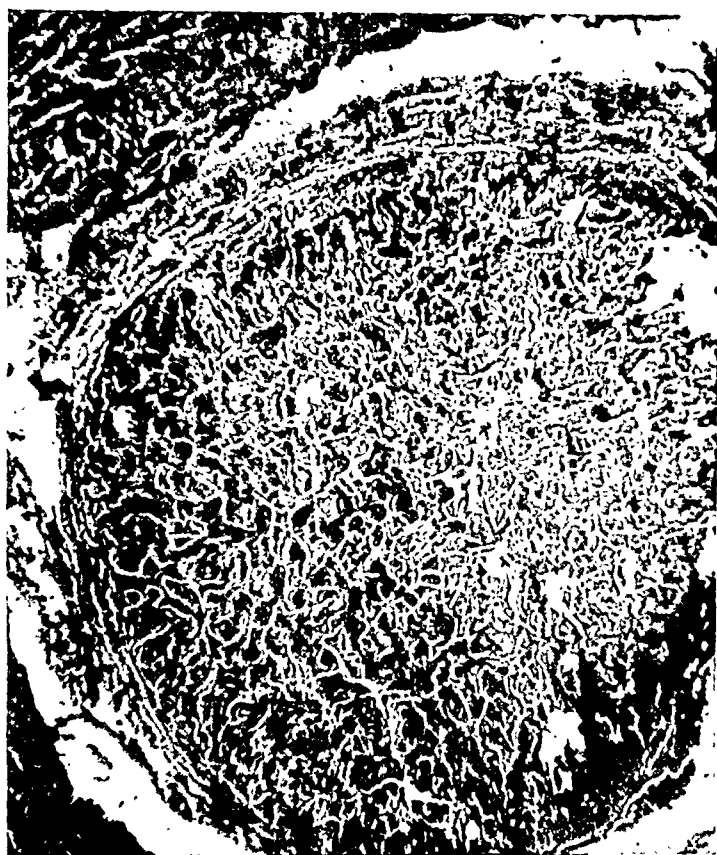


Fig. 5.—Photomicrograph showing section of abnormal optic nerve by which a victim was identified (Fig. 4).

achieved were due to the cooperation among all those involved. The most important evidence for the identification was contributed by the recognition of property and valuables in 32 cases, by dental studies in 25, by roentgenogram comparisons in 19, by pathology and medical histories in 16, and by fingerprints in 6 cases. In 10 cases property and valuables were the only evidence, and the dental findings were the sole basis for identification in 4 cases. In only one case did the medical evidence alone prove the identity. It would appear that property and dental studies were preeminent, but this deduction must be modified with respect to the following

facts. The investigation of each case was closed when sufficient evidence for identification was produced. In the last 42 cases, the really difficult ones, which were the subject of the most prolonged search, autopsy and x-ray were the most important factors in identification in nine instances each, whereas dental evidence was of value in only three, and property in only two. No matter how these figures reflect the relative merits of the different identification methods, they deal only with the solution of a small number of cases, and this review discloses that in the majority of cases the different mode of study made their significant contributions when used in conjunction with each other. Dental evidence was used in 72 cases, autopsy in 70, property in 53, roentgenograms in 38, and fingerprints in 13. In 50 cases the assistance of the Canadian and American Red Cross was a major contribution. It is obvious, therefore, that no one form of examination could have resolved the situation by itself, but, on the other hand, the combined efforts of all these different groups met with almost perfect results.

In this general account of the medical aspects of the "Noronic" identification, further observations on all the different types of investigation must, of necessity, have a bearing on the scheme as a whole, and yet to enlarge on them would be beyond the scope of this report. Indeed, the radiologists,⁷ the dentists,⁸ the dactylographers,⁹ the police, and the Red Cross⁹ either have reported or are on the point of publishing their methods and experiences, and the full particulars are to be found in their special periodicals. However, as the radiologic study is new and falls within the realms of medicine, it is permissible to comment briefly upon it. Antemortem films on 35 of the missing persons were received, and by comparison with the roentgenograms of the bodies 24 positive identifications were made. Confirmatory but inconclusive evidence was forthcoming in five more cases. The limitations of this method have already been alluded to, and the destruction of bony details by fire and the necessity for antemortem films are the important ones. Within these bounds, however, identification by roentgenogram comparison has been established as an absolute criterion. The pathologists acted as coordinators of the entire project and took full charge of the mortuary and the investigation, thereby suppressing the chaotic tendencies of the situation in its earlier hours. For the first three weeks every department in the committee was fully occupied in making successful identifications with the evidence they were producing, but, as the problem became more difficult and their solutions seemed unlikely, the pathologists, by repeatedly probing every source of information, provided the stimulus and the momentum that carried the project to its conclusion.

In the retrospective consideration of the "Noronic" studies, an account of the mistakes by the committee is as enlightening as its successes. In the identification of the dead there are always a number of pitfalls to be avoided, and, when so many mutilated bodies are concerned, these difficulties are multiplied. Although the Medical Identification Committee was aware of many of these, almost all of them were encountered, and

7. Singleton, A. C.: Roentgenological Identification of Victims of the Noronic Disaster, *Am. J. Roentgenol.* 60: 375, 1951.

8. Borland, O. E.: Identification in the Noronic Disaster, *Proceedings of the International Association for Identification in its 35th Annual Convention, 1950, Youngstown, Ohio, United Printing Company.*

9. National Disaster Institute, Canadian Red Cross, Toronto, 1949.

takes were made owing to failure to recognize them, or because circumstances made such mistakes unavoidable. A number of mistakes had already been made before the committee was organized. The removal of the bodies from the ship without taking a record of the site on the ship where the body was found was a definite mistake in technique, and yet, at the time, such documentation would not have been practical and, in the final analysis, no harm was done to the scheme. Admitting relatives to the mortuary, and permitting them to handle the bodies and property without proper supervision was another mistake that had to be rectified by the Medical Identification Committee. Nothing was gained by allowing the relatives to roam among these badly burned bodies. Two of the cases illustrate how the Medical Identification Committee paid the high cost of experience. The first is that of the body of a man who was identified by his two sons purely on their supposed recognition of a chip in a denture taken from the body. This happened on the day after the fire, just as the committee was starting its work. After the body had arrived for burial in Detroit, fingerprint studies were made, and they pointed out an error in identification. This body had to be returned to the mortuary. The correct body for this particular missing person was found shortly afterward. The dental features, the physical features, including an indirect inguinal hernia, and the fingerprints all proved the correct identification. This mistake illustrated not only the value of taking time to check the fingerprint studies but also the fallacy of accepting the recognition of relatives of mutilated bodies. In a second case the death certificate was issued for a woman missing in the fire on the basis of the finding of her social security card and the keys to her house, together with a portion of an arm at the site of the cabin on the ship which she occupied. Later, when her body was identified, there was considerable reluctance on the part of the family to accept the identification, mainly because they had already conducted a funeral for this person. The identification of this particular body was actually delayed by a mistake in taking for granted that parts of bodies belonged with a body near which they were found. While medical, dental, x-ray, and property evidence all were consistent with the identification of the particular woman, fingerprint evidence was repeatedly at odds, until it was discovered that the fingerprints were made from the hand that was with the body, but not attached to it. Actually the body from which the hand had come had been previously identified as somebody else. Such mistakes would seem easy to forestall, and yet, in the disturbed atmosphere under which the whole "Noronic" disaster investigation had to be conducted, they were inevitable. The commoner mistakes were made when the Identification Committee was rushed by situations beyond its control, and, as the errors came to light, the jurisdiction of the Identification Committee was strengthened, and interferences disappeared.

SUMMARY AND CONCLUSIONS

The identification of all but 3 of 119 persons who died in the fire that gutted the steamship "Noronic" represents an outstanding achievement, and the arduous medical

investigation by which it was accomplished has no precedent. Most of the bodies were absolutely unrecognizable. The facial features were wiped out, the skin was burned away, many limbs were missing, the viscera were shrivelled, and the clothing frazzled. So severely damaged were the bodies that few distinguishing characteristics remained, and the difficulties to be resolved far exceeded the capacity of the accepted procedures in the science of identification. These problems required a much broader approach, the basis of which was the comparison of all the information gathered on the missing persons with the facts gained by examination of the bodies. The responsibility for the collection and the complex analyses of the disaster rested on the pathologist.

The crossword puzzle charts and the other methods they developed for the utilization of this information were the key to the ultimate success of the project. The ordinary techniques in the science of identification were made use of, and an addition to the armamentarium was developed when the comparison of roentgenograms of the bodies with those of the missing persons proved their identity beyond question. Recognition of property on the bodies, fingerprint studies of the F. B. I. and the Toronto police, the autopsies and the medical inquiries of the pathologists, examinations made by the dentists—all were signal contributions to the identification, but it was through a combined effort of the entire Medical Identification Committee that the results were obtained. Teletype communication with centers throughout the United States and Canada, provided by the Red Cross, and the assistance they gave in all phases of the investigation, were an asset without which the project could never have been completed.

The Medical Identification Committee for the "Noronic" disaster has demonstrated that, no matter how badly charred or mutilated human bodies may be, their identity can be established by careful and prolonged medical investigation.

100 College St. (Dr. Brown).

New Problems in Treatment of Infectious Diseases.—Among the problems which confront us in the treatment of infections today, the following seem to be the most important: First is the increasing prevalence of infections caused by bacteria resistant to our present antibiotic drugs. This increase has not occurred in all bacterial infections. The most striking and most disturbing is the rising incidence of penicillin-resistant staphylococcal infections. This increase is thought to be due to the gradual reduction in numbers of naturally sensitive strains, rather than to the development of acquired resistance. A second problem is the occasional occurrence during antibiotic therapy of complicating infections caused by bacteria insensitive to the antibiotic being used, sometimes by microorganisms usually regarded as nonpathogenic. When such infections begin, for example, in the pharynx, they may result from a change in the bacterial flora of the throat, that is to say, from a disturbance of the equilibrium maintained by the bacterial antagonisms within the normal flora. Finally, infection may become a serious complication during treatment with ACTH or cortisone, presumably because these drugs interfere with the host's defensive response to bacterial invasion.—C. Phillip Miller, M.D., *New Problems in the Treatment of Infectious Diseases, Annals of Internal Medicine*, October, 1951.

EFFECT OF ACTH AND CORTISONE ON RHEUMATIC CARDITIS

OBSERVATIONS ON EIGHTEEN CASES

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In May, 1949, Hench and his co-workers¹ published their first paper on the treatment of acute rheumatic fever with cortisone and corticotropin (ACTH). These authors found that the effect on fever, polyarthritis, general "toxicity," and the erythrocyte sedimentation rate was striking, and these results have now been amply confirmed.² In this preliminary report Hench and his associates stated that the effect on rheumatic carditis was difficult to evaluate. In the opinion of those authors, patients receiving hormone therapy would have to be observed for many months before it could be determined whether chronic organic injury to the heart valves or myocardium had been prevented or decreased.

PLAN OF STUDY

In order to determine the effect of corticotropin and cortisone on rheumatic carditis, patients with rheumatic fever who had definite symptoms and signs of cardiac involvement were selected. The results obtained in 16 children, 1 adolescent, and 1 adult are reported. Twelve of these 18 patients were admitted during their first attack, and 6 gave a history of one or more antecedent rheumatic episodes.

Criteria for the Diagnosis of Carditis.—The diagnosis was made on the basis of the presence of one or more of the following symptoms: pericardial friction rub or effusion, roentgenographic evidence of change in the size or contour of the heart, congestive failure in children, the appearance of new murmurs, heart sounds of poor qual-

ity, gallop rhythm, and tachycardia in the absence of fever. None of the patients included in this report had a significant prolongation of the PR interval.

Therapeutic Regimen.—Four of the 18 patients received a single course of corticotropin (Cases 1, 3, 14, and 16), and 2 patients (Cases 6 and 8), a single course of cortisone. It was found that the acute symptoms of rheumatic fever (fever, "toxicity," and polyarthritis) subsided more quickly with corticotropin than with cortisone (throughout this study cortisone was administered by intramuscular injection). On the other hand, side-effects such as retention of sodium and water and loss of potassium were less marked in patients receiving cortisone. In four instances, therefore, corticotropin was given for three or four days and then followed by a longer course of cortisone (Cases 2, 4, 7, and 11). Patients who had relapses or failed to respond to cortisone were given one or two courses of corticotropin (Cases 9, 12, 13, and 18). One patient (Case 10), who showed only slight improvement after one course of corticotropin was given a second course for four days, followed by cortisone for 23 days. One patient (Case 15), who showed sodium and water retention after 16 days of corticotropin therapy, was changed to cortisone.

The eosinophil response was studied both in patients receiving corticotropin and in those receiving cortisone. A count was made before therapy was begun and approximately four hours after the initial injection of the hormone. A reduction of more than 50% in the number of eosinophils was obtained in the 15 cases in which it was studied. The range in the number of eosinophils was then followed throughout the period of therapy. The eosinophil response to cortisone was of the same order of magnitude as that to corticotropin.

Criteria for Evaluating the Effect of Hormone Therapy on Carditis.—An attempt was made to analyze the effect on the various aspects of cardiac involvement, including pericarditis, myocarditis, and endocarditis. In pericarditis the well-established criteria for improvement are disappearance of the pericardial friction rub, change in contour of the cardiac silhouette on roentgenographic examination, return of elevated ST segments to the isoelectric position, and the reversion of the T wave to normal in the electrocardiogram. Decrease in endocarditis due to valvular inflammation is indicated by the disappearance of newly developed murmurs or by a reduction in the intensity and transmission of the mitral systolic murmur. Objective findings of subsiding myocarditis are a roentgenologic decrease in the size of the heart in the absence of pericardial effusion and in children the disappearance of signs of congestive failure, with or without digitalization and diuretics. Congestive failure due to severe rheumatic infections, in contrast to that caused by mechanical

Dr. Harrison F. Wood of the Rockefeller Institute supplied the immune rabbit serum used for the C-reactive protein test.

The case protocols have been omitted from THE JOURNAL for lack of space but are included in an appendix to the authors' reprints.

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factors, often fails to respond to digitalis and mercurials. Other findings, some of which are more subjective, include an improvement in the quality of heart sounds and a reduction in what is usually described as cardiac "over-activity," indicated by the disappearance of gallop rhythm and tachycardia and a decrease in the lability of the cardiac rate.

RESULTS

For purposes of evaluation the 12 patients treated during their first rheumatic attack were divided into three groups. Group 1 received hormone therapy 8 to 14 days following the onset of rheumatic manifestations, Group 2 received therapy 35 to 52 days after onset, and Group 3 had had active or low-grade rheumatic fever for periods varying from 2 to eight months before receiving therapy. Since the results obtained in Groups 1 and 2 are similar, data on the eight cases included in these two groups are presented in Table 1 and on Group 3 in Table 2. The

treatment was continued more than six weeks. L. Z., on the other hand, was not acutely ill. He had apical systolic and diastolic murmurs, tachycardia, heart sounds of poor quality, and a labile cardiac rate. In addition to carditis he had mild chorea. During the first week of treatment tachycardia subsided, and the heart sounds improved but did not become normal. The lability of the cardiac rate persisted, and there was no change in the murmurs. The choreiform movements subsided completely. During the second and third weeks of therapy there was no further improvement in the carditis, and administration of corticotropin was therefore discontinued. Signs of activity then decreased gradually, the apical diastolic murmur disappeared eight weeks after treatment was stopped, and the rheumatic process was considered to be inactive.

B. L. (Case 4) was the youngest and most critically ill patient in Group 1. She had severe congestive failure,

TABLE 1.—Eight Patients Receiving Hormone Therapy Eight to Fifty-two Days After Onset of First Attack

Case	Age, Yr.	Days from Onset to Treatment	Therapy				Active Carditis		Follow-up	
			Hormone *	Days Treated	Total Dose, Mg.	Maximum Daily Dose, Mg.	Persistence of, or Time Required for Subsidence		After Therapy, Mo.	Cardiac Status ‡
							During Therapy	After Therapy		
Group 1										
1.....	9	8	ACTH	46	1,160	60	2 wk.	Inactive	9	Inactive; EH, MI
2.....	4	9	ACTH	3	180	60	4 wk.	Inactive	5	Inactive; SI EH, MI
3.....	5	14	Cortisone	34	3,250	100				
3.....	5	14	ACTH	21	935	60	Active	8 wk.	7	Inactive; SI EH, MI
4.....	2	14	ACTH	4	180	60	Active	9 wk.	5	Inactive; EH, MI, MS
4.....	2	14	Cortisone	12	7,100	200				
Group 2										
5.....	8	35	ACTH	23	970	60	3 wk.	Inactive	7	Inactive; SI EH, MI, AI
6.....	7	35	Cortisone	47	4,425	100 †	3 wk.	Inactive	2	Inactive; EH, MI, MS
7.....	7	39	ACTH	3	300	100	Active	6 wk.	4	Inactive; EH, MI, MS, AI
7.....	7	39	Cortisone	18	7,750	200				
8.....	3	52	Cortisone	27	2,610	100 ‡	Active	8 wk.	7	Inactive; EH, MI, MS

* ACTH = corticotropin.
† This patient received 300 mg. on the first day and 200 mg. on the second day.
‡ This patient received 200 mg. on the first day.
§ SI = slightly; EH = enlarged heart; MI = mitral insufficiency; MS = mitral stenosis; AI = aortic insufficiency.

courses of the six patients who had a history of previous rheumatic attacks are presented in Table 3 and are arranged according to the length of time that elapsed from onset to treatment.

Brief summaries of each case appear in the appendix. Only pertinent laboratory data, such as the C-reactive protein test,³ the erythrocyte sedimentation rate (Westergren), the eosinophil response to the first injection of hormone, the range in the number of eosinophils during therapy, and the roentgenographic findings, are included. More detailed reports and discussion of the effects of corticotropin and cortisone on the erythrocyte sedimentation rate and on the C-reactive protein response are reported elsewhere.⁴

Group 1.—The first four patients shown in Table 1 were treated within 14 days or less of the onset of the first attack of rheumatic fever. C. M. and L. Z. (Cases 1 and 3) both received corticotropin. In the former carditis subsided during therapy, whereas in the latter activity persisted. C. M. was acutely ill with pericarditis and severe extensive polyarthritis, and, although the carditis became inactive after two weeks of therapy,

which subsided only after digitalis and meralluride injection (mercuhydrin sodium solution[®]) were added to hormone therapy. In this patient hormone therapy was considered a lifesaving measure, because in a child of this age digitalis and meralluride injection often fail to control heart failure. This child received a total of 180 mg. of corticotropin and over 7 gm. of cortisone, yet, in spite of a prolonged period of treatment and high dosage, active carditis persisted. Therapy was discontinued because of the marked side-effects of fluid retention, abdominal distention, adiposity, and furunculosis. Six weeks after treatment was stopped, in addition to the apical systolic murmur that was present on admission, an apical diastolic murmur became audible and has

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persisted. The rheumatic process remained active eight weeks after therapy was discontinued. The follow-up examinations five to nine months after treatment was discontinued show that hormone therapy, instituted shortly after onset of the first rheumatic attack, had failed to prevent organic heart disease in the first four patients in this group. Three had definite and one questionable cardiac enlargement.

Group 2.—As far as subsidence of rheumatic activity was concerned, essentially similar results were obtained in the children included in Group 1 and in Group 2. In two of the patients carditis subsided during therapy, and in two it persisted for six to eight weeks after treatment was discontinued. Patient V. D. (Case 5) was acutely and critically ill with pericarditis and congestive failure. A dramatic response was obtained with cortico-

nodules decreased in size and number in 10 days, but a few small nodules persisted more than six weeks. In spite of large dosage, rheumatic activity persisted without therapy. There was no change in the apical systolic and diastolic murmurs, and the aortic diastolic murmur became consistently audible. Moon face and fluid retention with scrotal edema developed, and therapy was continued. Activity gradually subsided six weeks after treatment was stopped. In this patient biopsies of nodules were taken before treatment and after 38 days of therapy. A comparison of the sections of these two nodules showed a striking difference; the nodule obtained before treatment showed confluent small areas of granular eosinophilous inflammation characterized by infiltration of polymorphous mononuclear cells, minute focal areas of altered collagen, and the formation of new blood vessels.

TABLE 2.—Four Patients Treated Two to Eight Months After Onset of First Rheumatic Attack

Case	Age, Yr.	Days from Onset to Treatment	Therapy				Active Carditis		Follow-up	
			Hormone *	Days Treated	Total Dose, Mg.	Maximum Daily Dose, Mg.	Persistence of, or Time Required for Subsidence		After Therapy, Mo.	Cardiac Status §
							During Therapy	After Therapy		
Group 3										
9.....	8	61	Cortisone	7 †	875	150	Active	Active	14	Inactive; EH, MS, AI
				(Relapse after 12 days; re-treated after 17 days)						
			ACTH	32	1,269	100	Active	7 wk.	..	
10.....	13	90	ACTH	38	1,160	75	Active	Active	4	Inactive; EH, MI, MS
				(No improvement; re-treated after 12 days)						
			ACTH	4	300	100	Active	5 wk.	..	
			Cortisone	23	3,000	200				
11.....	6	105	ACTH	3	180	60	Active	Active	4	Inactive; EH, AI
			Cortisone	26	3,600	200				
				(No improvement; re-treated after 7 days)						
			ACTH	31	5,560	250	Active	7 wk.	..	
				(Rebound after 3 days; subsided without treatment)						
.....	5	240	Cortisone	27	2,900	100 ‡	Active	Active	3	Active; EH, MS
				(No improvement; re-treated after 11 days)						
			ACTH	10	835	100	Active	Active	..	
				(No improvement; re-treated after 32 days)						
			ACTH	28	4,960	320	Active	Active	..	

* ACTH = corticotropin.
† Cortisone discontinued because of increasing heart failure.
‡ This patient received 200 mg. on the first day.
§ EH = enlarged heart; MI = mitral insufficiency; MS = mitral stenosis; AI = aortic insufficiency.

tropin. Congestive failure subsided without digitalis or mercurials, and the rheumatic process became inactive within three weeks. Patients K. S. and D. E. (Cases 6 and 8), in contrast to patient V. D., were not acutely ill. In patient D. E. rheumatic activity did not subside with therapy. During the first eight days of treatment tachycardia decreased and the quality of heart sounds improved but did not become normal. Tachycardia and lability of the cardiac rate persisted. After 27 days therapy was stopped because there was no further improvement and severe furunculosis had developed. Carditis subsided gradually, and eight weeks later the rheumatic process was considered to be inactive. In Case 6 carditis subsided more rapidly, and it is possible that a similar result might have been obtained in Case 8 if larger doses had been used.

Patient J. M. (Case 7) was acutely ill. He had erythema marginatum, apical systolic and diastolic murmurs, an inconstant aortic diastolic murmur, and multiple nodules. He was given corticotropin during the first three days, followed by cortisone for 46 days. The

nodule obtained after treatment showed very prominent areas of altered collagen and almost no cellular reaction.

The follow-up examinations of the four patients in Group 2 two to seven months after treatment showed that hormone therapy administered during the course of their first attack of rheumatic fever had failed to prevent organic heart disease. In Group 2, in contrast to Group 1, however, therapy was not instituted until five to seven and one-half weeks after onset, and it seems possible that during this interval the rheumatic infection may have caused irreversible damage. As shown in Table 1, the valvular lesions resulting from rheumatic carditis were more severe in Group 2 than in Group 1.

Group 3.—The first attacks of rheumatic fever in the four patients of Group 3 presented in Table 2 were characterized by continuously active or low-grade rheumatic fever of two to eight months' duration prior to treatment. The response to hormone therapy in this group was less pronounced than in the patients treated earlier in the course of their disease (Table 1).

In the first of these four patients therapy was discontinued after seven days because fluid retention developed and heart failure increased. This patient's congestive failure was controlled with meralluride injection. Twelve days later he relapsed and was re-treated. Signs of active carditis persisted during the second course of therapy and did not subside until seven weeks after treatment had been stopped. In two children, although they were treated for 38 and 29 days, respectively,

sleeping pulse rate again rose sharply. That the rheumatic process was still very active was indicated by the fact that the results of the C-reactive protein test, which had become negative while the patient was receiving 320 mg. of corticotropin daily, again became strongly positive five days after therapy was discontinued.

The follow-up examinations three to fourteen months after therapy was discontinued showed that these four patients had organic heart disease. However, in spite of

TABLE 3.—Six Patients with Histories of Previous Rheumatic Attacks Treated 6 to 280 Days After Onset of Current Attack

Case	Age, Yr.	Previous Attacks	Cardiac Diagnosis on Admission *	Days from Onset to Treatment	Therapy				Active Carditis Persistence of, or Time Required for, Subsidence, Weeks		Follow-Up	
					Me. Men-ment †	Days Treated	Total Dose, Mg.	Max. Daily Dose, Mg.	During Therapy	After Therapy	After Therapy, Mo.	Cardiac Status *
13	12	2	Mod. EH, MI, MS, AI, AS	6	Cortisone (Relapse after 10 days; re-treated after 12 days)	44	4,500	100	Active	Active	..	
					ACTH	4	300	100				
					Cortisone	17	2,500	200	Active	10	4	Inactive; Mod. EH, MI, MS, AI, AS
14	9	1	Sl. EH, MI, MS	11	ACTH	9 ‡	540	80	Active	8	5	Inactive; Sl. EH, MI, MS
15	20	1	Mod. EH, MI, MS	13	ACTH	16	1,265	100	Active	Active	3	Active; Mod. EH, MI, MS
16	12	1	Mod. EH, MI, MS	23	Cortisone	28	3,875	200	Active	Active	7	Inactive; Mod. EH, MI, MS
17	15	10 §	Sl. EH, MI	37	ACTH	3	300	100	Inactive	Active	..	
					Cortisone (Relapse after 8 days)	17	2,800	200				
					Sod. salicyl.	23		9,000	1	Inactive	..	
18	9	2	Marked EH, MI, MS	270	Cortisone (No improvement; re-treated after 30 days)	20	1,030	100	Active	Active	..	Active; marked EH, MI, MS
					ACTH	13	520	40	Active	Active	12	

* Mod. = moderately; Sl. = slightly; EH = enlarged heart; MI = mitral insufficiency; MS = mitral stenosis; AI = aortic insufficiency; AS = aortic stenosis.

† ACTH = corticotropin; Sod. salicyl. = sodium salicylate.

‡ Discharged at mother's request.

§ One attack of carditis followed by multiple attacks of mild polyarthritis.

TABLE 4.—Effects of Hormone Therapy on the Signs of Carditis

Case	Initial Attacks												Recurrent Attacks					
	1	2	3	4	5	6	7	8	9 †	10 †	11 †	12 †	13 †	14	15	16	17 §	18
Pericarditis	A	...	...	...	A	A	...	...	A	...	...	...	A	A	A	A	...	A
Congestive failure	...	A	...	A	A	...	...	...	A	...	...	A	...	...	...	...	...	AP
Cardiac enlargement *	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	A	AP
Murmurs																		
Mitral systolic	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP
Mitral diastolic	...	...	AP	...	A	AP	AP	...	AP	AP	A	AP	AP	AP	AP	AP	...	...
Aortic diastolic	...	...	...	...	AP	...	AP	...	AP	AP	AP	...	AP	...	...	...	AP	...
Aortic systolic	...	...	...	...	...	...	...	...	...	...	...	...	AP	...	...	...	...	...
Poor quality heart sound	A	A	AP	AP	A	A	A	AP	A	A	A	AP	A	AP	A	A	...	AP
"Overactivity"																		
Gallop	...	A	...	A	A	A	A	...	A	AP	A	AP	...	A	A	...	A	...
Tachycardia	A	A	A	AP	A	A	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	...	AP
Labile rate	A	A	AP	AP	A	A	AP	AP	AP	AP	AP	AP	AP	AP	AP	AP	...	AP
Nodules	...	...	...	...	...	...	A	...	A	A	...	...	...	...	...	...	...	...

A = Finding present before therapy.

P = Finding still present three weeks after complete cessation of therapy.

* Enlargement exclusive of that due to pericardial effusion.

† These patients received two courses of hormone therapy.

‡ This patient received three courses of hormone therapy.

§ This patient received one course of hormone therapy and one course of salicylate therapy.

carditis persisted and they were therefore given a second course of therapy. In both these children signs of active carditis did not subside until several weeks after the second course had been discontinued. In the fourth patient carditis persisted during three separate courses of therapy. Because no response was obtained with the first two courses, massive doses of corticotropin (320 mg. daily) were tried. With this dosage the sleeping pulse of this patient became normal for the first time. However, severe side-effects, including moon face, abdominal distention, adiposity, hyperpigmentation, and hirsutism, developed. Corticotropin, therefore, was gradually reduced to 60 mg. daily. With this dose the

the prolonged period during which active carditis had persisted in these patients there was no further increase in the size of the heart.

Patients with Previous Rheumatic Attacks.—Three of the patients who had histories of previous rheumatic episodes (Table 3) were treated within 13 days or less of onset of their current attack. In patient P. L. (Case 13) carditis appeared to have become inactive after three weeks of therapy. Treatment was continued for an additional three weeks. Ten days after therapy was discontinued, however, a severe relapse of carditis and polyarthritis developed. A second course of therapy was given during which, in contrast to the first, carditis per-

sisted. Therapy was discontinued after 20 days because there was no progressive improvement and pronounced side-effects had developed. Carditis then subsided gradually and was considered to be inactive 10 weeks after treatment was stopped. V. S. (Case 15) received corticotropin for 16 days and was then changed to cortisone because of fluid retention. In patient H. C. (Case 17) carditis was considered to have become inactive after 20 days of treatment, and therapy was therefore discontinued. Eight days later, however, a relapse of polyarthritides developed, which subsided promptly with salicylate therapy. There was no recurrence of carditis, and the rheumatic process was considered to be inactive after 23 days, when administration of sodium salicylate was discontinued. Patient M. B. (Case 18) had had severe

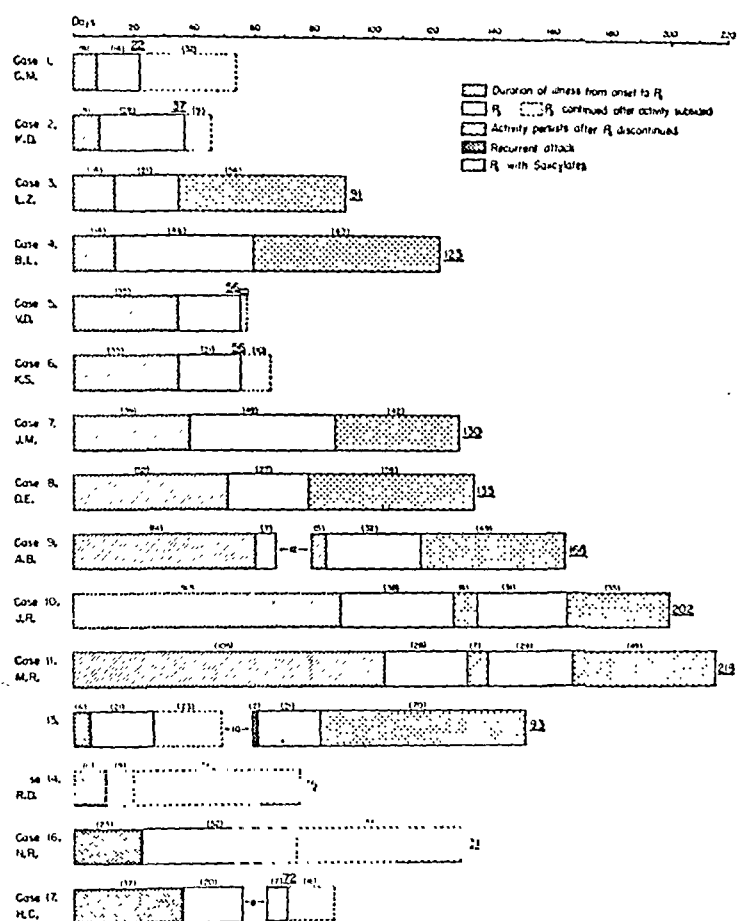


Chart showing course of 15 patients in whom carditis became inactive during or following treatment with cortisone or corticotropin.

polycyclic carditis for eight months prior to admission. Hormone therapy was instituted because of an acute exacerbation that increased the congestive failure. In the light of our subsequent experience, considering the severity and duration of the symptoms in this case, the dosage of both cortisone and corticotropin was probably inadequate. Laboratory as well as clinical evidence of continued rheumatic activity persisted during both courses of therapy.

Immediate Effect on Carditis.—The effect of hormone therapy on the persistence or subsidence of the various manifestations of carditis in the 18 cases reported in this paper is summarized in Table 4. The results were evaluated three weeks after complete cessation of therapy. This period of time was considered adequate to allow for the possible occurrence of symptoms due merely to the withdrawal of hormones. As shown in Table 4 the two aspects of carditis that apparently responded favor-

ably to hormone therapy were pericarditis and congestive failure. The one patient (Case 18) in whom cardiac decompensation did not disappear on therapy had severe heart disease with marked cardiac enlargement. This patient's C-reactive protein test and erythrocyte sedimentation rate did not become normal with therapy, suggesting that larger doses should have been tried.

In the absence of pericardial effusion, none of the 12 patients treated during their first attack of rheumatic fever showed a decrease in heart size. This was true in patients in whom the signs of carditis subsided during therapy as well as in those in whom rheumatic activity decreased gradually after therapy had been discontinued. In the group of patients who had had previous rheumatic attacks it was impossible to be sure that cardiac enlargement had not been caused by preceding rheumatic episodes. Aside from slight decrease in size attributed to the reabsorption of pericardial effusions, with one exception (Case 17), no significant change in cardiac enlargement was observed. A slight but definite decrease in size was noted in Case 17 after one week of therapy.

There was little change in the murmurs in the group of children treated during their first attack. Two children lost apical mid-diastolic murmurs, but in both these patients (Cases 5 and 11) aortic diastolic murmurs persisted. The murmurs remained unchanged in the six patients who had a history of previous rheumatic attack or well-established rheumatic heart disease on admission.

The quality of the heart sounds in most instances showed a definite improvement during therapy. In 6 of the 18 cases, although the heart sounds improved, they were not considered to be normal three weeks after therapy was discontinued. In most patients gallop rhythm disappeared rapidly. Tachycardia in the absence of fever and lability of the cardiac rate were the signs of carditis that persisted most frequently.

Effect on Nodules.—Three of the 18 patients had nodules. In Case 7 the number and size of the nodule decreased in 10 days. However, a few small nodules persisted for more than six weeks. A. B. (Case 9) had only two small nodules, which had almost disappeared before therapy was begun. J. R. (Case 10) had numerous nodules, which had been decreasing in size and number for two weeks prior to admission. All the nodules disappeared in 10 days with therapy. Although their disappearance appeared to be accelerated, it was impossible to be sure that the nodules might not have disappeared in the same length of time without hormone therapy.

Rebound Phenomena.—In spite of the fact that the doses of corticotropin and cortisone were reduced gradually, most of the patients showed an increased erythrocyte sedimentation rate and in many instances results of the C-reactive protein test also became positive again shortly after therapy was discontinued. These abnormal laboratory findings subsided without further treatment within a period of three weeks.^{1b} In one patient (Case 11) fever developed after the second course of therapy but this also subsided spontaneously.

Side-Effects.—With the exception of one patient who was treated for only nine days, all the patients showed some signs of hyperadrenalism. These side-effects occurred with both corticotropin and cortisone and were

most marked in patients receiving prolonged treatment or massive doses. Moon face, acneform eruption, abdominal distention, adiposity, furunculosis, and fluid retention were observed most frequently. Striae and hirsutism were less common. Transient tremors that subsided while therapy was continued developed in three patients. Hyperpigmentation developed in one child while he was receiving massive doses. Aside from mild insomnia in one child, no mental symptoms developed. All the side-effects were reversible and disappeared gradually after cessation of therapy.

COMMENT

The value of corticotropin and cortisone in the treatment of rheumatic fever can be determined first by its immediate effect on the manifestations of carditis and second by a long-range study to determine whether ultimate cardiac damage is prevented or its extent decreased. In accord with the observations of other workers, it was found that corticotropin and cortisone produced a prompt improvement in the general condition of the patients. The temperature decreased, "toxicity" disappeared, and joint manifestations subsided. Various abnormal laboratory findings (results of the C-reactive protein test, the erythrocyte sedimentation rate, and gamma globulin) tended to become normal. These effects were most striking in acutely ill, febrile patients. They were obtained with both corticotropin and cortisone but occurred more quickly with corticotropin.

In this series of 18 cases the manifestations of carditis that apparently responded most favorably were pericarditis and congestive failure precipitated by severe rheumatic myocarditis. In evaluating any new therapeutic agent in the treatment of rheumatic fever, however, the great variability of the disease must be borne in mind constantly. Although our data suggest that pericarditis was favorably affected by corticotropin and cortisone, the persistence of this manifestation of rheumatic carditis is known to be extremely variable. In this series, therefore, we are not certain that the disappearance of pericarditis was accelerated.

For many years there has been a divergence of opinion in regard to the treatment of congestive failure occurring during the course of rheumatic fever. In such cases often little or no response is obtained with salicylates, and many observers believe that digitalis is of doubtful value. Six of our 18 patients had signs of heart failure, which in 5 instances subsided during therapy. Two of these six children were critically ill, and it was our impression that in these two patients hormone therapy had been a lifesaving measure.

Disappearance of gallop rhythm and improvement in the quality of the heart sounds were observed in most of our cases. Tachycardia in the absence of fever and lability of the cardiac rate were the two signs of carditis that showed the least response to hormone therapy. In this series of patients disappearance of murmurs and a decrease in cardiac enlargement, exclusive of that due to reabsorption of pericardial fluid, were rarely observed.

It was often difficult in acutely ill patients to evaluate to what extent changes in the cardiac findings were due to the antipyretic effect of corticotropin or cortisone. With the subsidence of fever, tachycardia usually de-

creased, and with the slowing of the cardiac rate the quality of the heart sounds tended to improve and gallop rhythm often disappeared. In patients with carditis who were afebrile or had only low-grade fever, the immediate response to hormone therapy was less marked than in acutely ill patients. Even in the absence of fever large doses of corticotropin and cortisone may induce bradycardia.¹ This effect is well illustrated in patient J. H. (Case 12). Only during his third course of treatment, while he was receiving massive doses of corticotropin (320 mg. daily), did his cardiac rate become normal for the first time, but as the dosage was decreased the tachycardia recurred.

In this series the length of treatment and dosage varied. Even in the cases in which relatively small amounts of corticotropin or cortisone were given, a reduction of more than 50% in the eosinophil count was obtained. In many instances therapy was discontinued, in spite of the fact that the carditis was considered to be active, either because there was no progressive clinical improvement or because of untoward reactions to the hormones. It is our impression that, if dosage is adequate to control fever and reduce the results of the laboratory tests indicative of inflammation (C-reactive protein test and the erythrocyte sedimentation rate) to normal, there is probably no advantage in using massive doses. The severity of the untoward reactions increased when very large doses were used. The rheumatic process subsided gradually over a varying period of time in most of the patients in whom carditis was considered to be active at the time therapy was discontinued. On the other hand, two patients whose rheumatic process was thought to have become inactive during therapy relapsed promptly when treatment was stopped. In one of these patients (Case 13), although treatment had been continued 44 days, carditis after relapse remained active during the second course of treatment and only subsided 10 weeks after therapy was finally discontinued. These observations suggest that the subsidence of rheumatic activity may have been a function of time rather than a direct effect of the hormones on the rheumatic process.

After an average period of six months following cessation of therapy in the 12 patients in this series treated during their first attack of rheumatic fever, lesions indicative of organic heart disease are still present. This is true in the four children receiving therapy within 14 days or less of onset as well as in those treated later in the course of their disease. Many more patients and longer periods of observation are needed to determine whether in less acutely ill patients corticotropin and cortisone significantly shorten the duration of carditis. Corticotropin and cortisone are known to suppress the inflammatory reaction to a variety of infective agents. It seems possible that in rheumatic fever these hormones, by suppressing the cellular reaction, may decrease the fibrotic scarring of the myocardium and endocardium. Furthermore, with improvement in the general condition of the patients, the natural healing processes may become effective sooner and terminate the rheumatic infection more promptly. Whether in this way or by some as yet unknown action corticotropin and cortisone minimize structural damage to the heart and thus reduce the incidence or severity of chronic heart disease cannot be answered at present.

SUMMARY

The results obtained with corticotropin and cortisone in 18 patients with severe rheumatic carditis are described. In all cases the clinical and laboratory signs of active carditis were unequivocal. The administration of corticotropin and cortisone was followed by a definite improvement in the general condition of all the patients. Fever decreased, "toxicity" disappeared, and joint manifestations subsided. This therapeutic effect was most striking in acutely ill patients.

Twelve patients were treated during their first rheumatic attack at varying intervals after the onset. Eight received a single course of therapy one to seven weeks following the first appearance of rheumatic manifestations. Active carditis subsided during treatment in four of these eight children, but in the other four clinical evidence of rheumatic activity persisted for six to nine weeks after cessation of therapy. The remaining four of these 12 patients were treated several months after onset. Three received two courses of therapy. However, carditis did not subside until five to seven weeks after the end of the second course. In the fourth child the

rheumatic process was still considered to be active after three courses. Observations made two to nine months after complete cessation of therapy showed that all 12 patients had murmurs indicative of organic heart disease. Cardiac enlargement was definite in all but one case.

Six patients with antecedent rheumatic heart disease were treated during recurrent attacks. Therapy was instituted at intervals varying from 1 to 38 weeks from onset. In two patients, signs of activity disappeared within three weeks after therapy was begun, but relapse occurred in both within 10 days after the hormones were withdrawn. In two patients, active carditis persisted for 9 and 14 weeks, respectively, and in two patients for longer than 16 weeks. Signs of hyperadrenalism were observed frequently but in every instance disappeared gradually after cessation of therapy.

In this group of patients it was not clear whether the use of corticotropin or cortisone significantly decreased the duration of active carditis or influenced cardiac damage. Further studies with a greater number of patients and prolonged periods of observations are necessary.

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EOSINOPHIL LEVELS AS AN INDEX OF ADRENAL RESPONSIVENESS

FACTORS THAT AFFECT VALUE OF EOSINOPHIL COUNTS

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Since its first recognition as a separate morphological entity in 1865 by Max Schultze, the eosinophil cell has been the subject of much investigation. Earlier workers sought to clarify its morphology and function. By 1888 observers were studying differential counts, and in the same year Mayet described his eosin-glycerin method. In the next few years methods requiring the use of a counting chamber were devised by many authors quoted by Rud,¹ but none was successful; these methods were superseded by Dunger's method in 1910, which met with competition from exponents of the smear technique.¹

The most exhaustive study in the field was done in Sweden by Rud from 1939 to 1943 and published in 1946-1947.¹ Here not only were attempts made to evaluate the methods of doing differential counts, but a study was made on the variation of the eosinophil count during the day, week, and seasons; the influence of position change, fasting, menstruation, sex, age, and constitutional type was also observed. After studying 550 subjects Rud concluded that his chamber method, using as a

diluent 0.1 cc. of 10% magdala red, 6 cc. of acetone, to 20 drops of 10% sodium carbonate solution, and 10 cc. of water, was superior to the smear method and that the eosinophil counts were reproducible, within a normal range, in the same subject from day to day and season to season, regardless of body position, menstruation, sex, age, and constitutional type. However, in many instances a drop occurred in the forenoon, with a rise later in the afternoon and night. This diurnal cycle was independent of food intake, but in a significant number of cases fasting caused the number of eosinophils to drop.

In the past few years attention has been focused again on eosinophil counts and their relation to adrenal function. Thorn and his co-workers² devised a test for adrenal responsiveness which in effect is a measure of eosinophil levels before and after a stimulating dose of corticotropin (ACTH), and many investigators using corticotropin and cortisone have adopted this test. Recently Fisher and Fisher³ studied eosinophil counts in normal subjects and found wide variations. They felt that this indicated that "it would be difficult to use this phenomenon as a sensitive indicator of pathologic variations." Because "Thorn's test" is done in the morning and forenoon hours of a fasting subject and because some investigators still use the smear method on finger or oxalated venous blood, it was felt that the question should be reevaluated.

METHODS

Two methods of determining the number of eosinophils were used.

1. In the chamber method a diluting fluid composed of equal parts of 0.1% phloxine and 0.1% methylene blue in propylene glycol was used.³ Blood from a finger puncture was drawn in

Damon Runyon Research Fellow.

Mrs. Betsy Bundy, Miss Miriam Gobstoo, and Miss Vivian Freeman gave technical assistance in this study.

From the Clinical Research Laboratories of the Jewish Memorial Hospital and the Department of Medicine, Tufts College Medical School.

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a standard white blood cell count pipet in the usual manner, using the fluid as a diluent. The pipet was shaken by hand for two minutes, and then four counting chambers were charged. The chambers were allowed to stand for 15 minutes, and then the eosinophils seen in the nine squares of each chamber were counted and averaged. The figure obtained was multiplied by the factor 22.2 to obtain the final eosinophil count. If the number in one chamber varied greatly from the results in the other three, this figure was not used in calculating the average.

2. A blood smear from a finger puncture was made on a glass slide and stained with Wright's stain. A white blood cell count was also done on the blood from the same puncture or on oxalated venous blood. Eight hundred white blood cells in two groups of 400 were counted and the number of eosinophils noted. Then the number of eosinophils per 100 cells was computed and multiplied by the average of four white blood cell chamber counts expressed in units of 100. The result gave the absolute figure of circulating eosinophils. If the distribution of eosinophils in either group of 400 cells was uneven, then an additional 400 or a total of 1,200 cells were counted and the eosinophils per 100 cells calculated accordingly.

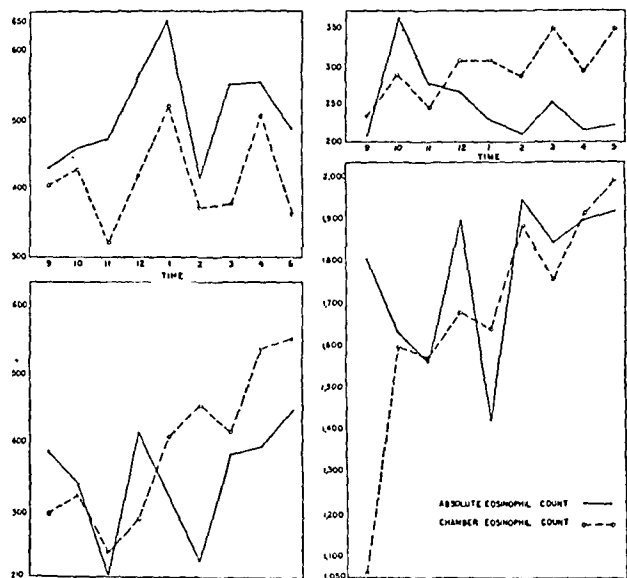


Chart 1.—Chart showing discrepancies between results of counts by chamber and smear methods expressed in eosinophils per cubic millimeter when only 400 cells were counted on the smears and only two chambers counted in the direct method of Randolph. Absolute eosinophil count indicates results obtained by counting eosinophils on the dry blood smear. Chamber eosinophil count indicates results obtained by counting eosinophils directly in the counting chamber. The time is expressed in hours from 9 a. m. to 5 p. m.

A total of 1,852 eosinophil counts were done, each checked by three persons. Seventeen normal subjects and 33 patients with various diseases were included in this study (39 women and 11 men). The age span was from 19 to 79 years. Diagnoses for the 33 patients included generalized arteriosclerosis, cerebrovascular accident, rheumatoid arthritis, carcinomas of various types, myasthenia gravis, fractured hip, syringomyelia, Paget's disease, Parkinson's disease, seborrheic dermatitis, multiple sclerosis, and progressive muscular atrophy.

PLAN OF STUDY

All counts were done by both the chamber method and the smear method from the same sample of blood. In 52 instances counts were computed in stages, i. e., two chambers or a group of 400 cells on smear were first taken, the absolute eosinophil count was made, and then the count was expanded to include four chambers and a group of 800 cells on smear. The final answers in each

group were compared with the results obtained by counting half as many cells. In 20 patients an eosinophil count was performed by the chamber method on oxalated venous blood and also on blood from a finger puncture done at the same time.

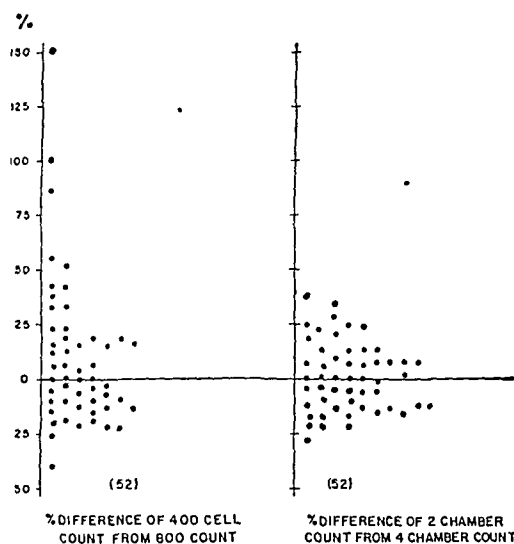


Chart 2.—Chart showing comparison of different results obtained by counting 400 cells or 800 cells on smears or by studying two chambers or four chambers using the direct method. Each dot represents one subject.

Forty-nine subjects who had been fasting since the previous evening were observed from 8 a. m. to 12 noon or from 9 a. m. to 1 p. m. Eosinophil counts were done either at 8 a. m. and 12 noon or at 9 a. m. and 1 p. m., the accepted hours for doing the Thorn test. A percentage drop in eosinophils of 50% or more has been considered a sign of intact adrenal function.

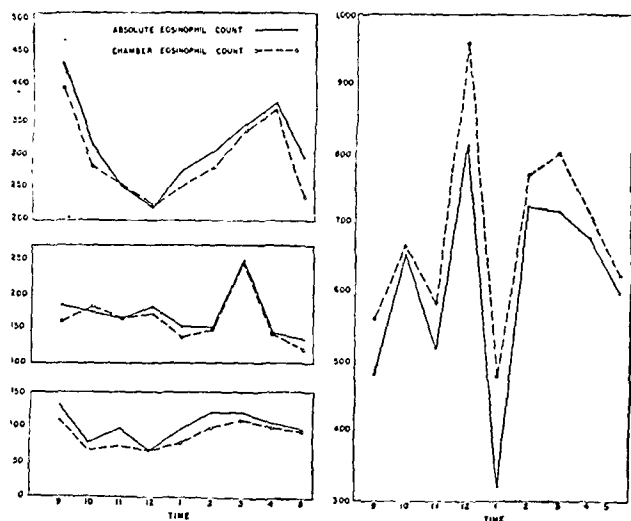


Chart 3.—Chart showing good correlation between chamber eosinophil counts and absolute eosinophil counts (obtained from blood smears) when 800 cells are counted on the smear, or when the eosinophils are counted directly in four chambers.

Fifty subjects (including the 49 who were observed while fasting) were allowed to eat according to their regular schedule, and eosinophil counts were again done at the same intervals. The same 49 subjects were again allowed to eat at their regular hours and the eosinophils were measured at 1 p. m. and 5 p. m.

One patient with rheumatoid arthritis who did not respond to corticotropin therapy but did respond to cortisone, one patient with panhypopituitarism, and four patients with Addison's disease were studied by hourly eosinophil counts throughout the day.

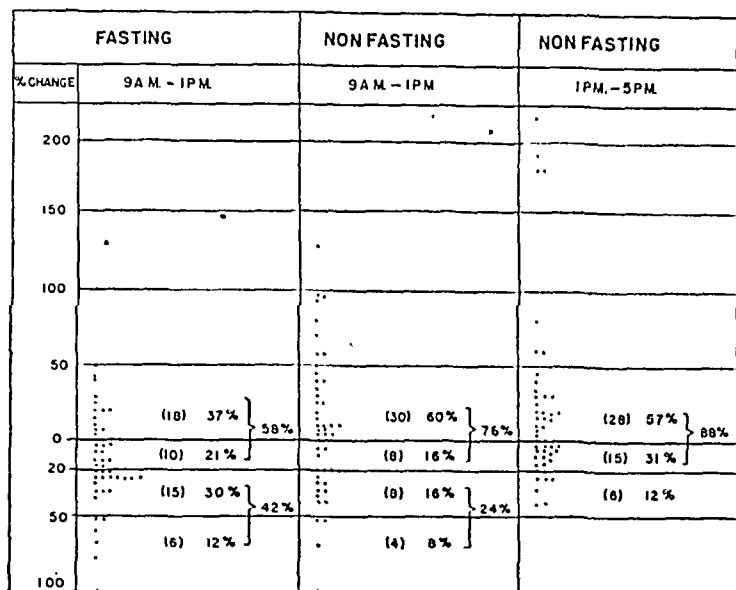


Chart 4.—Chart showing changes in eosinophil counts (by percentages of initial counts) occurring during fasting or normal food intake. The figures in parentheses represent the number of patients for each percentage. Each dot represents one subject.

One three subjects a Thorn test was done while they were fasting every Tuesday morning and while they were consuming food every Friday afternoon for four weeks in order to determine the reproducibility of the eosinophil response to 25 mg. of corticotropin (Armour) in the same subject.

RESULTS

1. In comparing the chamber method with the smear method it soon became obvious that if only two chambers were counted and only 400 cells were included in the

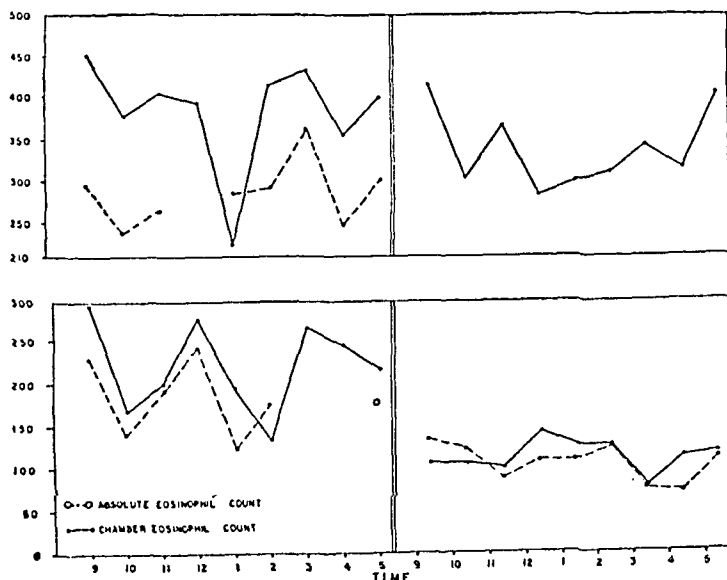


Chart 5.—Chart showing the fluctuation of eosinophils per cubic millimeter in four patients with Addison's disease with counts done hourly from 9 a. m. to 5 p. m. Absolute eosinophil count refers to counts done using the smear method, and chamber eosinophil count refers to the direct counting of the eosinophils in the counting chamber.

smear method, the results were not consistent. Chart 1 shows the results when counts were done every hour by both methods. The inconsistency is shown more pointedly in Chart 2, which gives the results when each count was done in two stages, counting first two chambers and

400 cells on each smear and then comparing the results obtained with those from the counts of four chambers and 800 cells on smears.

The 400-cell preliminary smear counts vary from -40% to +150% from the final 800-cell counts, while the two-chamber counts vary from -27% to +29% from the final four-chamber counts. Thus at the first stage the chamber count is more reliable than the smear count. However, when four chambers and 800 cells were counted, the two methods paralleled each other quite well (Chart 3). This was confirmed in many isolated counts done by both methods. Of 50 curves of results of counts done hourly during the day, 61% showed absolute counts by the smear method which were higher than the corresponding chamber counts. In 640 isolated counts 65% of the counts done by the smear method were higher than the chamber counts. The higher the eosinophil count, the greater was the possibility of a wider numerical difference. Except in rare instances, however, either type of count would have been adequate for clinical purposes.

Comparison of Repeated Tests in Same Subjects at Different Times of Different Days During Fasting or When Eating *

Fasting 9 A. M.-1 P. M.		Nonfasting 1 P. M.-5 P. M.
Cancer of Thyroid		
46.4		55.3
39.2		42.8
36.4		30.0
17.1		28.4
Cancer of Breast		
86.4		50.5
51.7		69.2
65.4		64.4
43.6		36.3
Normal Subject		
78.3		35.6
40.8		74.4
40.8		78.8
63.4		63.7

* The figures express decrease in eosinophils in percentages of pretest values.

2. When results obtained in freely flowing blood from finger punctures were compared with those obtained from oxalated venous blood, the finger blood gave higher results in 59% of the cases, while in 19% the results were identical. The variation between the results of counts seemed to be no different from that to be expected from the methodology in itself. Curves showing counts done every hour during the day were not identical when the counts were repeated on the same individual on different days, indicating that the daily pattern may vary widely.

3. It was found that 37% of the fasting subjects (Chart 4) had percentage changes of 0 and above, 21% had percentage changes between 0 and -20%, 30% had percentage changes of -20% to -50%, and 12% had changes below -50%. In this group of fasting patients 12% showed drops of the eosinophil counts, as if they had received corticotropin and had given a normal response to a Thorn test, and 30% of them had drops of from -20% to -50%.

4. In the group which ate at regular times and were tested from 9 a. m. to 1 p. m., 60% had percentage changes of 0 or above, 16% had falls between 0 to

—20%, 16% between —20% to —50%, and 8% had falls below —50%. Allowing the patients to eat resulted in a reduction of the number of those whose eosinophil counts decreased spontaneously.

5. When the same patients ate on their regular schedule and were tested from 1 p. m. to 5 p. m., 57% had percentage changes of 0 and above, 31% between 0 and —20%, 12% between —20% and —50%, and none of more than 50%. It is noteworthy that in none of these subjects did the number of eosinophils fall by a percentage that would simulate a normal response to corticotropin, and only six patients had falls between —20% to —50%. Three of these six had percentage changes of —22%.

6. The patient with rheumatoid arthritis who responded to cortisone and not to corticotropin showed a constant eosinophil level throughout the day. One patient with panhypopituitarism also showed little diurnal change of the eosinophil levels. Three of the four patients with Addison's disease, however, showed diurnal curves that fluctuated in the same manner as those of the other subjects, including normal subjects (Chart 5).

7. The results of this study of repeated Thorn tests with the Chamber method are summarized in the accompanying table. It can be seen that an individual occasionally responds differently at different times when a Thorn test is done, and may sometimes fall from the "responsive" into the "nonresponsive" range or vice versa. It would therefore seem that a nonresponsive test should not be regarded as conclusive until it has been repeated with the same results.

COMMENT AND SUMMARY

From this study it appears that either the chamber count or the smear method for the counting of eosinophils may be used equally well for clinical purposes. The two methods parallel each other, provided that four chambers are counted and averaged or 800 cells are counted on the smear. The choice of method depends on the local circumstances. In a laboratory where many eosinophil

counts are done by the same personnel, the chamber method is probably preferable because it is more rapid. A technician will develop the proficiency required for good results with this method. For those who do only occasional eosinophil counts it is perhaps advisable to use the smear method, because most technicians are experienced in the preparation of blood smears and in doing differential white blood cell counts. The results obtained from freely flowing finger blood or from oxalated venous blood do not differ significantly, but either one or the other should be used consistently.

Because it has been shown that fasting alone will cause a drop in number of circulating eosinophils, and since it has also been demonstrated that even in nonfasting subjects eosinophils drop fairly consistently in the forenoon and rise later in the afternoon, it is felt that the Thorn test may be more sensitive as an index of adrenal responsiveness if done on a nonfasting patient from 1 p. m. to 5 p. m. This has been true in my own, still limited, experience with 30 such tests in the afternoon.

It is interesting to note that in patients with Addison's disease daily curves of the number of eosinophils resembled those obtained in the group without adrenal disease. This contrasted with what might have been expected from the flat curves obtained in a patient with panhypopituitarism and in a patient with rheumatoid arthritis who did not respond to corticotropin. It suggests either that patients with Addison's disease have adrenal remnants still capable of being stimulated by certain stresses⁴ or that mechanisms exist for the control of eosinophil levels other than cortisone-like substances. Such mechanisms might also account in part for the fact that the same subject will respond differently to the same stimulating dose of corticotropin at different times in respect to the level of the circulating eosinophils.

30 Bennet St.

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THE SULFONAMIDES AND ANTIBIOTICS IN TRACHOMA

Arthur A. Siniscal, M.D., Rolla, Mo.

The following preparations were used and the results observed in a series of over 3,500 patients with trachoma at the Missouri Trachoma Hospital during 1941-1951: sulfanilamide, sulfapyridine, sulfathiazole, sulfathiazine, sulfacetamide ("albugid"), sodium sulfacetamide ("albugid" soluble), sulfamylon® (4-amino-2-methyl benzene sulfonamide hydrochloride), diacetylaminoazotoluene (prontosil®), combisul® (a combination of sulfadiazine, sulfamerazine, and sulfathiazole), sulfisoxazole diethanolamine (gantrisin®), penicillin, bacitracin, streptomycin, chloramphenicol (chloromycetin®), aureomycin, and terramycin. Some of the sulfonamide drugs were used in tablet form for internal medication and others in aqueous solution, as drops for local instillation into the conjunctival sac. Both of these methods were usually combined, and an overnight coating of the sulfa ointment

was also used. The antibiotics were prepared in fresh, buffered, aqueous solutions daily, from crystalline powders supplied in sterile vials, and used for topical application every two hours. Only surface applications of antibiotics were used, since it was felt that systemic injections of adequate dosage do not produce measurable concentrations in the ocular, and particularly the conjunctival, tissues and fluids. Moreover, it was felt that, in trachoma at least, subconjunctival injections of antibiotics were not justifiable, since simpler methods appeared as effective.

Medical Director, Missouri Trachoma Hospital.

Read before the Section on Ophthalmology at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 14, 1951.

THE SULFONAMIDES

All the sulfonamides named in this report were found to be beneficial in trachoma. Their action was generally mild, or bland, on the conjunctiva. Some sulfonamides, such as sulfanilamide, diacetylaminoazotoluene, sulfacetamide, and sodium sulfacetamide, caused toxicity; others were not highly soluble and afforded little concentration of solid when in solution. For these reasons, the early sulfonamides (previous to 1945) were discarded in favor of the more recent, highly soluble drugs, such as gantrisin,[®] sodium sulfacetamide, sulfadiazine, and combisul.[®] Since 1945, these products have been found to be the most effective and least toxic of the available sulfonamides.

Sodium sulfacetamide forms a stable, highly soluble, aqueous ophthalmic solution and, if used in no higher than a 10% concentration, is effective in trachoma with only occasional toxic side reaction. Stronger solutions are ineffective because of irritation. Gantrisin[®] is a newer, highly soluble, well-buffered, aqueous ophthalmic solution and is the ideal sulfonamide in trachoma because of its minimal toxicity, blandness of action, and therapeutic effectivity. It is used in 4.3% solution (optimal for local use), and as a tablet of 7.7 grains (0.5 gm.) for internal use. Neither tablet nor solution is toxic. Combisul,[®] consisting of equal parts by weight of sulfadiazine, sulfamerazine, and sulfathiazole, is very effective in trachoma when used as tablets of 0.5 gm. for internal medication. Its toxicity is minimal, and it requires no alkalization for use. Sulfamylon[®] hydrochloride, 1% solution, is a well-buffered, aqueous, aromatic ophthalmic solution but was not found to be so effective or so bland as gantrisin,[®] 4%, and sodium sulfacetamide, 10%. Sodium sulfacetamide, 10% ointment, and gantrisin,[®] 10% ophthalmic ointment, form stable emollients for coating the conjunctiva during the night. Treatment at Missouri Trachoma Hospital was a three-way attack: (1) local instillation every two hours of gantrisin,[®] 4.3% solution, daily, for from 10 days to 3 weeks (occasionally, sodium sulfacetamide, 10% solution, was used instead); (2) internal medication with gantrisin[®] given orally in four divided daily doses, according to age and weight for the first seven days; and (3) coating the conjunctival surfaces nightly with gantrisin,[®] 10% ophthalmic ointment or sodium sulfacetamide during the entire period of treatment.

Early subsidence of all inflammatory symptoms, gradual resolution of pannus if incipient, and the rapid disappearance of photophobia and blepharospasm resulted. Mild entropion and trichiasis showed improvement by unfolding of the beginning incurvation of lids. Advanced cicatricial entropion does not improve. Early pannus formations were fairly well resolved. Moderately advanced vascularizations did not resolve. Ulcerations improved as far as the general condition improved. Opacification was not affected, except as the general inflammatory condition subsided. Cicatrization, once established, was not affected. Early entropion that was of blepharospastic nature improved only after sulfonamide treatment.

THE ANTIBIOTICS

Penicillin, bacitracin, streptomycin, chloramphenicol, aureomycin, and terramycin, in this order, were used during the past five years at the Missouri Trachoma Hospital, but with disappointing results, as a specific cure for trachoma. The antibiotics have no effect on trachoma per se, but, for clearing up secondary infections associated with trachoma, they are excellent.

Cases of trachoma with concomitant blepharitis, purulent blennorrheas, pneumococcic ulcers, or staphylococcic infections of the tear sac responded quickly and well to irrigations with penicillin, terramycin, aureomycin, and chloramphenicol, and excellent results were also obtained in these infections with ointments of bacitracin, penicillin, and terramycin. However, no direct effect upon the underlying trachomatous condition itself was observed to follow with antibiotics. Trachoma patient treated with antibiotic solutions and ointments every day for several weeks and longer failed to show any improvement in clearing of incipient pannus, relief from turbulence of the retrotarsal fold, resolution of granules, or even from the increased lacrimation and itching that is almost always present in all trachoma. When secondary infections complicated trachoma, antibiotics relieved the symptoms to some degree and produced a partial subsidence of inflammation. Very purulent secretions cleared remarkably within a few days after treatment. In such cases, the underlying trachoma seemed improved, but this was only because superimposed infection was alleviated and controlled by application of antibiotic solutions or ointments.

COMMENT

There has been much discussion during the past decade as to whether the sulfonamides and the antibiotics have a specific effect on the virus in trachoma. The majority of investigators claim the sulfonamides do have a specific effect. Thygeson, Sorsby, Wilson, Bietti, Richards, Forster, Poleff, Freyche, Loe, and Cosgrove believe they do. Thygeson states that, in cases in which specific inclusion bodies were found previous to administration of sulfonamides, they could not be found after treatment with this drug. Others have demonstrated that Prowaz inclusion bodies disappear from the conjunctiva in a few days or more following sulfonamide treatment. Sorsby concludes from his observations that the sulfonamides are specific against the virus of trachoma and not merely against any associated secondary infections. I believe that further bacteriologic research will conclusively prove specificity of sulfonamides for the virus of trachoma.

The antibiotics, too, are at present under fire regarding their specificity in trachoma. Many foreign observers and some in America believe them to be specific. Some workers, however, draw conclusions too soon, before they have properly evaluated the type of infection at the time and number of cases under study. A long time must elapse and a large number of cases must be studied before it is possible to decide whether any agent is

specific drug for trachoma. I do not believe that trachoma per se is affected materially by aureomycin or any other antibiotic used in this work. I think some foreign observers are led to believe that antibiotics are beneficial because of the existence of florid secondary infections almost always attending trachoma in the Near East and Orient. In Egypt, for instance, trachoma is almost always secondarily infected with pneumococci, gonococci, or Koch-Weeks infection, and often trachomas preceded by one of these conditions. Since antibiotics are effective generally against these infections, a rapid improvement of the over-all clinical picture results, and the credit is given essentially to trachomacidal action. It would not be too difficult to draw premature conclusions regarding specificity for aureomycin and other antibiotics. In the Missouri Ozarks region, trachoma infection is usually unattended with secondary infections; thus, antibiotics have had their opportunity to prove themselves, if effective, in cases of pure trachoma, but have failed. In the Orient, on the other hand, because of the many, consistent, almost constant, secondary and mixed infections present with trachoma, the antibiotics have had a better chance to show dramatic effects and give an impression of cure. Not until antibiotics can relieve primary, uncomplicated trachoma infection, with inflammation, turgescence, incipient pannus, and photophobia, or can be proved bacteriologically to have a direct viricidal action, will it be possible to draw accurate conclusions in this matter.

CONCLUSIONS

1. The primary role of the sulfonamides in the treatment of trachoma is established. They stand as first therapeutic choice because of their relative mildness of action and apparent specificity against the trachoma virus.
2. Antibiotics are of secondary help in clearing the common pus-producing organisms attendant to trachoma, and thus serve to shorten the total morbidity period of this disease.
3. Although therapeutic agents that give speedier effects and possess greater flexibility would be desirable, to date the sulfonamides stand superior to all other therapeutic agents used thus far in this ocular disease.

Collagen Diseases and Cortisone.—The two syndromes—rheumatoid arthritis and rheumatic fever—are not far separated in their nature and in their response to cortisone. Similar comparisons hold for some of the other collagen diseases. Perhaps the most hopeful aspect of the study is the wide portion of clinical medicine which is influenced by this hormone. The unexpected and far-reaching influence of cortisone on many diseases may be produced through its control of some causative agent which is common to all of them. The nature of this agent is unknown, but I agree . . . that the hypothesis of the adaptation syndrome of Selye . . . is not acceptable. Today it can be said that cortisone will relieve the pain and symptoms of rheumatoid arthritis, and it constitutes a life-saving measure for other syndromes, but to the clinician interested in research it will be a key which will unlock the doors of barriers and reveal secrets long hidden.—Edward C. Kendall, Ph.D., *The Adrenal Cortex and Rheumatoid Arthritis*, *British Medical Journal*, Dec. 1, 1951.

CLINICAL NOTES

PROPYLTHIOURACIL-INDUCED AGRANULOCYTOSIS, TOXIC HEPATITIS, AND DEATH

REPORT OF A CASE

Arthur R. Colwell Jr., M.D.

Don E. Sando, M.D.

and

Samuel J. Lang, M.D., Evanston, Ill.

Because of its therapeutic effect and minimal toxicity, propylthiouracil has become the drug of choice in the treatment of hyperthyroidism. Leukopenia developed in only 10 of 672 patients who received the drug in preparation for thyroidectomy.¹ Recently, however, administration of propylthiouracil has been reported to cause death or severe disability in a few cases. Livingston and Livingston² reported a nonfatal case of toxic hepatitis following treatment with the drug. Two other fatalities from agranulocytosis have been described previously in the literature.³ This is a report of a third death due to agranulocytosis, associated with early toxic hepatitis, following the administration of propylthiouracil.

REPORT OF CASE

History.—A white woman, a secretary, aged 60, was admitted to Evanston Hospital on Aug. 17, 1950. Until two weeks before admission she had been perfectly well. At that time she noticed palpitation and a "tightness" in the chest on reclining or following exertion. A week later she had shortness of breath on walking to work in the morning, followed by ankle edema in the evening. There was an occasional nonproductive cough, but no orthopnea nor paroxysmal nocturnal dyspnea. The patient had also noticed nervousness, irritability, and a slight tremor of the hands in the two weeks prior to admission. The past and family history were noncontributory, and history by systems disclosed no abnormalities.

Physical Examination.—The patient was a nervous, pale, somewhat undernourished woman, with an anxious expression. The oral temperature was 99 F; the pulse rate 120, and the blood pressure 150/70 mm. Hg. The skin was warm and moist. There was no exophthalmos nor lid lag. The fundi were normal. The teeth were in poor condition. No mass was palpable in the region of the thyroid gland. Crackling rales were present at both lung bases. There was a sinus tachycardia, which was not changed by rest nor exercise; the heart was not enlarged, and the sounds were normal. The liver was not palpable. There was 1+ pitting ankle edema.

Hospital Course.—The clinical impression was that the patient had arteriosclerotic heart disease with congestive failure. She was digitalized with 1.2 mg. of digitoxin, given in divided doses. This had no effect on the tachycardia, and digitoxin was discontinued on the third day because of nausea and vomiting. A low-sodium diet, 0.2 gm. of aminophylline three times daily, and 1 gm. of ammonium chloride five times daily were also administered. On the second hospital day, 0.2 gm. of quinidine sulfate

From the Department of Medicine, Evanston Hospital.

1. Bartels, E. C.: Agranulocytosis During Propylthiouracil Therapy, *Am. J. Med.* 5: 48-52 (July) 1948.

2. Livingston, H. J., and Livingston, S. F.: Agranulocytosis and Hepatocellular Jaundice: Toxic Reactions Following Propylthiouracil Therapy, *J. A. M. A.* 135: 422-425 (Oct. 18) 1947.

3. (a) Juliar, B., and Harris, T. L.: Fatal Agranulocytosis Occurring During Propylthiouracil Therapy: Report of Case, *J. A. M. A.* 139: 646-647 (March 5) 1949. (b) Beebe, R. T.; Propp, S.; McClintock, J. C., and Versaci, A.: Fatal Agranulocytosis During Treatment of Toxic Goiter with Propylthiouracil, *Ann. Int. Med.* 34: 1035-1040 (April) 1951.

was administered three times daily because of a transient episode of auricular fibrillation. The heart size was normal on a roentgenogram, and an electrocardiogram indicated only tachycardia and digitalis effect. Because of the lack of response to digitalis, hyperthyroidism was suspected. The blood cholesterol level was 149 mg. per 100 cc., the basal metabolic rate was +40%. Propylthiouracil therapy, 300 mg. given daily in three doses, was instituted on Sept. 1, and potassium iodide, 5 minims (0.308 cc.) daily, on Sept. 7. The pulse rate continued to vary between 100 and 110. A second trial with digitoxin only produced further nausea and vomiting without slowing the pulse rate. By Sept. 5 the blood cholesterol had risen to 222 mg. per 100 cc., and the basal metabolic rate was +6%. The hemoglobin value was 11 gm. (71%), red blood cell count 3,620,000, and repeated white blood cell counts from Sept. 5 to Sept. 15 varied between 3,500 and 5,000. On x-ray examination, the gallbladder, esophagus, stomach, duodenum, and colon were normal. There was no evidence of a substernal thyroid. The patient was discharged on Sept. 19, somewhat improved, with instructions to take 300 mg. of propylthiouracil daily. A white blood cell count reported after discharge was 2,550 cells.

Readmission.—On Oct. 2, 13 days after discharge, the patient was readmitted to the hospital. She had undertaken a 100-mile motor trip one week after discharge. While she was away, malaise, fever, chills, anorexia, and a nonproductive cough had developed. All medication had been voluntarily discontinued on Sept. 29. On readmission, the oral temperature was 103.2 F, pulse rate 120 and irregular, respiration rate 20, and blood pressure 80/40 mm. Hg. First and second degree burns from locally applied heat were present on the abdomen and chest. A few dry rales were heard in the left lung base. There were alternating periods of auricular fibrillation and flutter. The red blood cell count was 2,900,000; the white blood cell count was 250. Treatment with 100,000 units of penicillin every three hours, morphine sulfate, intravenous fluids, quinidine, and blood transfusions was instituted.

Laboratory findings the day after admission (following two transfusions) were as follows: hemoglobin, 11.5 gm. (74%); red blood cells, 3,500,000; white blood cells, 2,380; polymorphonuclear leukocytes, 7; lymphocytes, 47; monocytes, 45; basophil, 1; and thrombocytes, 64,000. The blood contained nonprotein nitrogen, 55.7 mg. per 100 cc.; total cholesterol, 216 mg.; cholesterol esters, 104 mg.; total serum proteins, 4.8 gm.; albumin, 3.1 gm.; globulin, 1.7 gm.; and total serum bilirubin, 10.9 mg. The thymol turbidity was 2.6 units, cephalin flocculation, 4+, and alkaline phosphatase, 1.7 Bodansky units. The urine showed 4+ albuminuria.

The day after readmission, the patient became clinically jaundiced. She complained of anorexia, dyspnea, nausea, mild cramping pains in the lower abdomen, and diarrhea with watery, greenish stools. The temperature remained at 102 F orally. An electrocardiogram showed auricular fibrillation, but on the following day the rhythm was normal. By auscultation, it was felt that there were intermittent periods of auricular fibrillation, auricular flutter, and regular sinus rhythm. The white blood cell count dropped to 1,200 and then to 700, with 4 polymorphonuclear leukocytes, 66 lymphocytes, and 30 monocytes. The red blood cell count was 3,490,000, with a hemoglobin level of 10.5 gm. per 100 cc. (68%) and 64,000 thrombocytes. The chest was normal on x-ray examination, but clinically there appeared to be pneumonia of both lower lobes. The patient died on Oct. 5, 1950. The clinical impression was that the patient had aplastic anemia and leukopenia due to propylthiouracil, upper respiratory infection with possible bronchopneumonia, and organic heart disease due to hyperthyroidism, with auricular fibrillation and flutter.

Autopsy.—The body was that of a well-developed, fairly well-nourished, white woman of 60 years, measuring 161 cm. in length and weighing an estimated 55 kg. The scleras and skin were markedly icteric, and there was slight pitting edema of both lower extremities. All serous surfaces were smooth, glistening, and yellowish.

The heart was moderately hypertrophied (330 gm. in weight), and there were minimal arteriosclerotic changes in the coronary arteries. The lungs were subcrepitant, and scattered throughout

the parenchyma were small, deep maroon, nodular areas. A moderate amount of frothy, yellow fluid could be expressed from the bronchioles. Sections of the lungs showed bronchopneumonia, characterized by early necrosis of the bronchioles surrounded by alveoli filled with red blood cells, lymphocytes, and bacteria. No polymorphonuclear cells were found. The presence of pigment-containing macrophages indicated chronic pulmonary congestion.

The liver weighed 1,620 gm. and had a normal brown color other than having a moderate "nutmeg" appearance, the sectioned surface appeared normal. Microscopically, there was a fairly marked loss of liver cord cells around the central vein but no evidence of focal areas of necrosis elsewhere, or biliary stasis. There was a moderate degree of fatty metamorphosis, and a few lymphocytes were seen in the periportal areas. These changes suggested early toxic hepatitis. The extrahepatic biliary tree was patent, and there were no lesions of the gallbladder. The spleen weighed 290 gm. The parenchyma was brown-red and friable, with a decrease in corpuscular markings. With the exception of a congenital double pelvis and double ureter on the left, the kidneys showed no lesions.

The appendix, which was lying medially and loosely adherent to the omentum, was edematous and reddened. The serosal surface was roughened, and several purple hemorrhagic blebs encircled the organ. Yellow-white coalescing patches surrounded by bright red hemorrhage covered the mucosal surface. There was a similar, though not so pronounced, appearance of the internal mucosa from the transverse colon through the rectum. These lesions in no place perforated the wall. Microscopic examination of all layers of the appendiceal wall showed marked hemorrhagic lymphocytic infiltration, and necrosis (severest in the muscular and submucosa). The lesions in the colon closely resembled those in the appendix; however, the muscular wall was slightly involved. In both organs, there were numerous bacilli and no polymorphonuclear leukocytes. These changes represented acute ulcerative appendicitis and colitis, which probably appeared terminally following the development of agranulocytosis.

The bone marrow showed a decrease, though not an absence of the cells of the granulocytic series, and only an occasional adult form was seen. Erythropoiesis was active. The thymic gland weighed 38 gm. and appeared grossly normal. On microscopic section, the gland showed marked epithelial hyperplasia characterized by numerous papillary infoldings into the lumen and reduction of colloid. This appearance might have been caused by treatment with propylthiouracil or by an increased secretion of thyroid hormone.

COMMENT

In our opinion, death in this case was due to a fulminating septicemia secondary to agranulocytosis which resulted from toxic suppression of the bone marrow by propylthiouracil. Contributing to the septicemia were the acute ulcerative appendicitis and colitis, as well as the pneumonia, which resulted from loss of the normal defense mechanisms against infection, attendant upon agranulocytosis. Whether the hepatitis was caused by propylthiouracil administration, by a virus infection contracted before admission to the hospital, or by terminal septicemia is difficult to determine, but the latter possibility seems most likely. Recovery from the cellular jaundice similar to that in Livingston's case might have occurred, if infection from other sources had not appeared and caused death. In our case the effects of propylthiouracil were irreversible, in spite of the fact that the drug had been discontinued a few days before death.

In addition to the case of agranulocytosis and jaundice from propylthiouracil previously mentioned,² several other cases of toxic hepatitis due to thiouracil poisoning

en reported.⁴ Of these cases, histological studies were possible in only two. Gargill and his co-workers,^{4b} in a section taken by biopsy 18 days after the onset of jaundice, found distention of the bile canaliculi and small thrombi, indicating acute biliary stasis. In an autopsy specimen taken 59 days after the onset of jaundice, Holoubek^{1c} described focal and central necrosis, as well as plugging of the bile canaliculi.

The histological findings in the liver of our patient are not remarkable. The loss of liver cord cells around the central veins was more marked than would be expected from chronic passive congestion and probably represented an early stage of toxic hepatitis. The minor degree of this change may be explained by the apparently short duration of hepatitis before death occurred.

SUMMARY

A third case of death from agranulocytosis due to propylthiouracil therapy is described. There was accompanying toxic hepatitis, apparently resulting from administration of propylthiouracil.

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COARCTATION OF AORTA WITH SURGICAL CORRECTION AT AGE FORTY

REPORT OF A CASE

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As a consequence of the demonstration by Crafoord,¹ Blalock,² and Gross³ that coarctation of the aorta in man is amenable to surgical cure, there is an increased interest and incentive in the diagnosis of what has previously been considered an incurable clinical curiosity. Gross⁴ has reported the results in 100 such patients operated on by him. Of these 100, 91 did not survive and 9 had only exploratory operations. Of the remaining 80, 71 were cured completely, 8 obtained satisfactory relief, and 1 had no relief.

There has been some question about operating on older people for the correction of coarctation of the aorta. Gross considered that the optimal age for performance of the procedure was between 6 and 20 years. He felt that in persons older than 25 the aorta was too arteriosclerotic for manipulation and suture. Clagett⁵ successfully performed a Blalock procedure on a 34-year-old man, the oldest patient with coarctation to have been operated on up to that time. In his discussion he stressed the disadvantages of operating on a patient that old because "there are rather severe arteriosclerotic changes in the vessels of persons who have had coarctation for a long period." Gross⁶ as late as 1949 mentioned that "some excellent results have been obtained in patients in the late twenties." His oldest patient up to that time had been 31 years old. In his later publication⁴ age is not mentioned. Blalock, in discussing Gross'⁶ paper, reported a successful operation in a man aged 41. He believed this patient was the oldest ever operated on for coarctation.

The purpose of this particular paper is to describe a patient with coarctation of the aorta successfully operated on at the age of 40. This patient presumably is the second one over the age of 40 to have had this operation.

REPORT OF A CASE

J. P., a white automobile plant superintendent, first learned that he had hypertension six years prior to this hospital admission. One year later a thymectomy was done at another hospital. In spite of the hypertension, he remained relatively asymptomatic until three months prior to admission, when he began to notice gradually increasing palpitation, sweats, and flushing of the face. There was a 15 lb. (6.8 kg.) weight loss. On questioning, the patient said that his feet had been cold for a number of years. The past history and family history were not relevant.

Examination revealed a well-developed, well-nourished adult with flushed facies, who appeared apprehensive but not ill. Blood pressure in the left arm was 174/102 and in the right arm 178/90. The radial pulse rates were equal, and the brachial pulses were easily visible. The femoral pulse was weak and exhibited a slow rise. The popliteal and dorsalis pedis pulses could not be felt, and a blood pressure in the legs was unobtainable. Both lower extremities were colder than normal.

There were minimal changes in the retinal vessels, including a slight increase in the light reflex of the arterioles and moderate arteriovenous nicking. The visual acuity ratio was 2:1. In the



Fig. 1.—Roentgenograms showing the heart to be of normal size. The aortic knob is not visible. Multiple notching of the inferior borders of the ribs is present.

neck a few posterior cervical nodes and gross pulsations in both supraclavicular areas were noted.

The left side of the thorax appeared more prominent than the right. On auscultation there was a loud systolic murmur that could be heard over the entire precordium. This murmur could be traced down along the right sternal border almost to the umbilicus and along the left sternal border to a point beyond the umbilicus. It could be heard, also, in the axillas and in the interscapular area. Pulsations could be felt in various areas of both the anterior and posterior chest fields, and in some of these areas they could be seen. No diastolic murmur was heard. The remainder of the physical examination disclosed no abnormalities.

The blood count showed 4,520,000 red blood cells and 7,800 white blood cells, with 66% segmented polymorphonuclear cells, 1% stab forms, 31% lymphocytes, 1% eosinophils, and 1%

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5. Clagett, O.: Coarctation of the Aorta: Surgical Aspects, *Proc. Staff Meet., Mayo Clin.* **22**: 131, 1947.

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monocytes. The hemoglobin value was 85% (Sahli). The Kahn reaction was negative. The urine had a specific gravity of 1.018 and contained an occasional white blood cell. The urine contained no albumin, glucose, casts, or red blood cells.

A urine concentration test showed a range of specific gravity from 1.008 to 1.020. The phenolsulfonphthalein excretion rate was 30% in 15 minutes and 50% in one-half hour. Urea clearance was 196% in the first specimen and 220% in the second. The nonprotein nitrogen concentration was 31.0 mg. per 100 cc. Serum protein level was 7.18 mg. per 100 cc.

Oscillometric readings were as follows: right wrist, $\frac{1}{2}$ unit; left wrist, $\frac{1}{2}$ unit; right calf, $1\frac{1}{2}$ units; left calf, 1 unit; right ankle, $\frac{1}{4}$ unit; and left ankle, $\frac{1}{4}$ unit.

A roentgenogram of the chest (Fig. 1) revealed normal lung fields and a normal-sized heart. The aortic knob prominence was absent. There was notching on the inferior margins of the ribs. An electrocardiogram was entirely normal.

On April 26, 1950, an operation was performed by Dr. Dewey Dodrill. A long parascapular incision was made on the left thorax, extending from about the level of the third thoracic vertebra midway between the spine and the vertebral border of the scapula downward, curving beneath the tip of the scapula and then anteriorly to reach the anterior axillary line. The musculature of the chest wall presented huge pulsating arteries, some as large as lead pencils, which had to be carefully isolated and

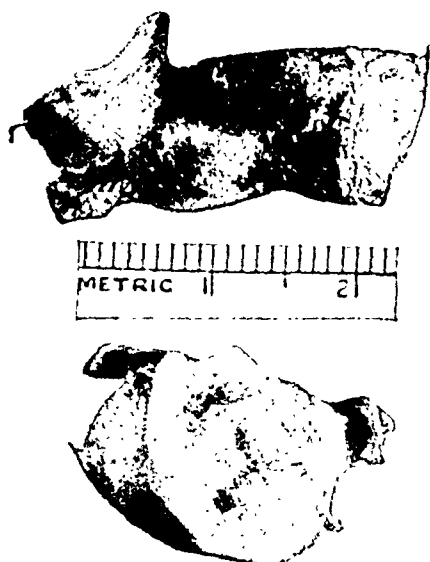


Fig. 2.—Two views of the excised segment of aorta. The lower view is looking into the lumen of the vessel, demonstrating that the aorta is completely occluded.

ligated with silk suture. The scapula was retracted, the fourth rib resected subperiosteally, and the pleural cavity entered.

When the lung was retracted downward and forward, the coarctation was found just distal to the left subclavian artery and was approximately 2 cm. in diameter. The left subclavian artery was almost 1 in. (2.5 cm.) in diameter; the pressure within it was very high. The adventitia of the aorta was incised, and then by blunt dissection the aorta was freed around the constricted area and from there proximally to a point beyond the origin of the left common carotid. Three sets of intercostal arteries had to be divided, all of which were hugely dilated. These entered the aorta just distal to the coarctation and carried blood from the collateral circulation to the lower thoracic aorta. It was noted that these collateral vessels were hard, rigid, and nonresilient, presumably because of atheromatous change. One of them was so friable that ligation was impossible, since the ligature cut right through its wall. This vessel was sewed with fine interrupted silk suture.

A modified Potts clamp was placed on the proximal portion of the aorta, which partially occluded the common carotid. This was unavoidable, since the subclavian and common carotid were very close together. A coarctation clamp was then placed on the distal aorta, after which the constricted area was resected. The ends of the aorta were approximated and sutured with 0000 arterial silk, with a continuous everting type of mattress suture which was interrupted at three points. No atheromatosis had been noted within the lumen of the aorta itself. The distal clamp

on the aorta was then released, revealing two small bleed points, which were controlled with interrupted silk sutures. The proximal clamp on the aorta was next released gradually over a period of five minutes. There was no precipitous fall in blood pressure as this latter clamp was released. The resected portion of the aorta was examined, and it was noted that its lumen was completely occluded.

During the operation the patient received 3,500 cc. of blood. His condition remained good throughout the procedure. The postoperative course was uneventful. On the day following surgery the blood pressure in the left arm was 148/118 and in the right arm 152/120, in the left leg 170/122 and in the right 168/124. The femoral pulses were increased, and the dorsalis pedis pulses were palpable for the first time. The precordial murmur gradually became fainter and finally disappeared. Sounds that had previously been heard over areas of collateral circulation (axillas, posterior chest, and abdomen) all disappeared. Oscillometric readings on the 20th postoperative day were as follows: right thigh, 4 units; right calf, $3\frac{1}{2}$ units; ankle, 1 unit; left thigh, 3 units; left calf, $1\frac{1}{2}$ units; and ankle, $\frac{3}{4}$ units. The color and temperature of the lower extremities had returned to normal. The patient was discharged from hospital on the 19th postoperative day.

When last seen, on June 23, 1950, the patient was entirely asymptomatic and had returned to his former employment. His blood pressure was 140/80, the pulse rate 88 per minute, and heart sounds normal. The lower extremities were entirely normal as to warmth, color, and freedom from symptoms. Pulses in the legs were full and adequate bilaterally.

SUMMARY

The factor of age with reference to the operability of coarctation of the aorta is discussed. Coarctation was successfully corrected by surgery in a man 40 years of age as described. This is believed to be the second case in the record in which a patient of 40 or over has had this condition with a successful outcome. It is noteworthy that in this patient, although the intercostal vessels were markedly sclerotic, the aorta itself was not atherosclerotic.

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RHINOSCLEROMA SUCCESSFULLY TREATED WITH STREPTOMYCIN

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Rhinoscleroma is not a common disease in the United States, but its study is of interest, since it is a severe progressive infection of disputed etiology.

Rhinoscleroma is widespread throughout Europe, Asia,^{1b} and Hawaii.² The condition is said to be most common in Central America.³ In the United States and Canada 102 cases had been reported by 1942; only 10 of the patients were native born.⁴

Rhinoscleroma begins as a nasal catarrh, some with a foul odor, and gradually progresses to a

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2. Crawford, H., and Gerundo, M.: Rhinoscleroma; Report on Two Cases Recognized in Hawaii, *Hawaii M. J.* 7: 23, 1947.

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4. Cunning, D., and Guerry, D.: Scleroma, *Arch. Otolaryng.* 34: 1942.

characterized by cartilage-like nodules that tend to occlude the nasal passages. Since Frisch⁵ in 1882 described an encapsulated gram-negative rod as the main cause of rhinoscleroma, there has been much discussion as to the actual significance of the organism. It has been impossible to fulfil Koch's postulates because the Frisch bacillus (now called *Klebsiella rhinoscleromatis*) has not produced rhinoscleroma when inoculated into experimental animals⁶; likewise, attempts to produce the disease in human volunteers have been unsuccessful.⁷ Such studies, together with the fact that *K. rhinoscleromatis* has been recovered from well persons,⁸ have led to the postulation that a virus may be the true causative agent of rhinoscleroma.

Our case is similar to another in which treatment was given the same year (1946), reported by New and others⁹; they reported an encouraging response to streptomycin therapy. Since that time five cases have been reported in the United States in which there was response to streptomycin or dihydrostreptomycin therapy.⁹ Also, three patients in Yugoslavia¹⁰ and one in France¹¹ have favorably responded to this antibiotic.

It has been possible to follow our patient for three years after initial treatment, thus affirming that arrest of the disease was apparently accomplished, not temporary remission. All the cases in which treatment was with streptomycin, since there was response to this therapy, give support to the belief that the Frisch bacillus is the etiological agent of the disease because the Frisch bacillus is a gram-negative rod showing in vitro sensitivity to streptomycin.

REPORT OF A CASE

A Latin American woman, 27, came to the office Aug. 27, 1946, with a complaint of nasal obstruction and severe sore throat. The patient had lived in south Texas all her life and had never visited Mexico. About two or three months previously she had noticed some difficulty in her nasal breathing, which was soon followed by a sore throat.

Examination revealed that the anterior nares were partially obstructed with granulosomatous tissue. The soft palate was markedly inflamed. This patient was seen on several occasions and finally consented to enter the hospital on Dec. 11, 1946. At this time the nose was completely occluded with granulosomatous tissue. There was a destructive lesion of the soft palate with complete loss of the uvula. Numerous sections were removed from both nostrils as well as from the soft palate and sent to the laboratory.

Pathologist's Report.—The specimen consisted of several pieces of tissue removed from within the nasal cavity. These varied considerably in size and shape. Each tissue had one border covered or partially covered by stratified squamous epithelium. This was somewhat atrophic with complete absence of the rete pegs. The stratum mucosum, including the basal cell layer, was uniform in structure. In the outer portion of the corium were many Mikulicz cells. These were large cells with small nuclei and foamy cytoplasm. With proper staining, small gram-negative rods could be seen within these cells. Many broad bands of connective tissue were scattered throughout this granuloma, in some areas completely replacing the other cellular elements. The majority of cells in this granulosomatous process were plasma cells. With these were some round and ovoid acidophilic structures called Russell bodies.

Russell bodies were found rather frequently in rhinoscleroma, and the presence of Mikulicz cells containing bacilli resembling those of the Frisch bacillus is diagnostic indication of the disease.

Bacteriologist's Report.—Acid fast smears for the leprosy bacillus were negative. Aerobic and anaerobic cultures showed

abundant growth of a gram-negative rod having a highly mucoid colony. Tests for Neufeld's reaction with anti-Friedlander serums types A, B, and C were negative. This lack of quellung and negative mouse pathogenicity tests ruled out the organism as a member of the Friedlander group. Culturally and biochemically the isolated organism is compatible with *K. rhinoscleromatis*, as described in Bergey's manual (fifth edition). Antibiotic sensitivity tests on the isolated organism showed it to be resistant to 10 whole units of penicillin per cubic centimeter. It was completely inhibited by 5 units of streptomycin per cubic centimeter and partially inhibited by 1 unit per cubic centimeter.

There were no reports of streptomycin having been used up to this time for the treatment of rhinoscleroma, but in view of the sensitivity tests, this antibiotic was chosen for therapeutic trial.¹²

The patient reentered the hospital on March 15, 1947. She was given a total of 28 gm. of streptomycin in ¼ gm. doses every four hours. At the end of the fifth day the lesion in the soft palate had completely healed. Cultures from the nares as well as the soft palate were taken repeatedly and were negative. At the end of six months and again at the end of three years no evidence of the organism was found in either cultures or sections. The patient was last seen on Feb. 8, 1950. At this time the palate was completely healed, and both nostrils were free of granulosomatous tissue. There was some constriction of both nares due to scar tissue but no evidence of a lesion.

COMMENT

In addition to the fact that rhinoscleroma responds to streptomycin therapy, there is another type of evidence which strongly supports the theory that rhinoscleroma is caused by the bacillus which bears its name. Complement fixing antibodies to this organism have been found in the majority of rhinoscleroma patients examined, and the complement fixation test is proving a practical method of diagnosing the condition.¹³

SUMMARY

A patient with rhinoscleroma treated with streptomycin showed clinical improvement within five days after the beginning of therapy, and cultures promptly became negative for *Klebsiella rhinoscleromatis*. Lesions did not recur during a subsequent three year period of observation. This dramatic response to streptomycin therapy in this patient and those mentioned elsewhere lends additional weight to other existing evidence that *Klebsiella rhinoscleromatis* is the causative agent in the disease from which it is named.

705 E. Houston St. (Dr. Russell).

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CONGENITAL ECTODERMAL DEFECT WITH AMASTIA

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Congenital ectodermal defect is a rare syndrome characterized by hypotrichosis, absence of sweat glands, absence of sebaceous glands, adontia or hypodontia, a characteristic facies, and, occasionally, absence of the mammary glands. About 80 such cases have been reported, but only 4 of these (all male) have had absence of the breasts and nipples.¹ The purpose of this report is to record a case of this variety.

A brief consideration of the clinical appearance of patients with ectodermal defect (Fig. 1) reveals a great similarity in their appearance. The skin is thin, dry, and glossy, and the facies is somewhat suggestive of congenital syphilis. Frontal bossing is prominent, the supra-orbital ridges are high and wide, the nasal bridge de-

a 30-year-old white man, a native of Venezuela, who had no nipples, but who had no other ectodermal defects. However, these cases are not instances of the syndrome of ectodermal defect.

REPORT OF A CASE

R. M., a Negro boy aged 16 months, was admitted to Gallinger Municipal Hospital on July 16, 1948, because of diarrhea and a positive Kahn reaction. The diarrhea responded to symptomatic therapy. Results of repeated serological tests for syphilis were negative, and the child was discharged without further treatment. He was admitted to Children's Hospital on Oct. 15, 1948, because of an upper respiratory infection. This infection was found to be tuberculous bronchopneumonia, an improvement followed treatment with streptomycin and dihydrostreptomycin. He was transferred to Glenn Dale Tuberculosis Sanatorium on Feb. 4, 1949, for convalescence.

History and Physical Examination.—The mother was treated for early latent syphilis during pregnancy with 3,000,000 units of penicillin in oil and wax; her last serological test for syphilis was still positive. The father was unknown. The mother knew of no inherited anomalies in her family. The child was obviously malnourished and had a very dry and scaly skin and scalp devoid of any hair, except fine lanugo fuzz. There were

Chief Features of Reported Cases of Ectodermal Defect with Amastia

Case	Author	Date	Sex	Hair	Teeth	Skin	Nose	Sweating	Nails
1	Hutchinson.....	1886	M	Alopecia except lanugo hair	"Tolerably normal"	Thin, wrinkled, "old-mannish"	Not described	Not stated	Spoon-shaped
2	Tendlau.....	1902	M	Partial alopecia; beard, axilla, and pubis normal	4 in upper jaw; none in lower	Dry, thin, and scaly	Saddle; atrophic mucous membrane	Absent	Normal
3	Kaalund-Jorgensen.....	1941	M	Alopecia except lanugo hair and eyelashes	13; some deformed	Thin, fine, and dry	Saddle; atrophic mucous membrane	Absent	Normal
4	Upshaw and Montgomery..	1949	M	Partial alopecia; beard normal	None	Keratoderma of palms and soles	Saddle; atrophic mucous membrane	Absent	Normal
5	Osbourn.....	1952	M	Alopecia except lanugo hair	None	Thin, dry, and scaly	Saddle	Absent	Normal

pressed, the lips thick and protruding, the teeth absent or deficient, and the nails normal or dystrophic. Cases have been reported of absence of mammary glands, chiefly in females, unassociated with any of the other stigmas of ectodermal defect. In a review of the literature 10 cases² of unilateral absence were found and five cases³ of bilateral absence. In addition, Dr. Robert Owen⁴ told me of a private patient whom he saw in 1950,

no eyebrows or eyelashes. The supraorbital ridges were prominent. The nasal bridge was depressed, the lips were thick and everted, and no teeth were present. The chest was smooth, with no evidence of breast tissue or nipples. The nails and extremities were normal.

Laboratory and Sweating Studies.—The Kahn reaction was 1+ in July, 1948; repeated tests gave negative results over the next eight months. The spinal fluid was within normal limits. Roentgenograms of the chest were consistent with the clinical (medical) diagnosis. A roentgenogram of the mouth area did not show any evidence of teeth or any tooth buds (Fig. 2). Biochemical studies could not be performed. The child had never been noted to sweat; when he was placed under a heat cradle for 10 minutes there was no sweating, but the body temperature rose about 1°F. Injection of pilocarpine and use of "quinizarin compound" (28% 2:6 disulphonic acid with sodium carbonate and corn starch) failed to produce any sweating on several areas of the

COMMENT

This case is the fifth to be reported in which absence of nipples and mammary glands is a part of the syndrome of congenital ectodermal defect. All the patients have been males; all have had absence of sweating and partial or complete absence of teeth. The chief features of the syndrome are listed in the table.

The clinical and pathological aspects of this syndrome have been adequately described in the excellent paper of Upshaw and Montgomery.¹⁰ The most disabling feature of the syndrome is the inability to sweat and the di-

Assistant Clinical Professor, the Department of Dermatology and Syphilology, Georgetown University School of Medicine.
The staff of the Tuberculosis Sanatorium (Glenn Dale Sanatorium), Glenn Dale, Md., particularly Dr. M. Weiss, assisted in the handling of this case.
1. (a) Hutchinson, J.: Congenital Absence of Hair and Mammary Glands, Proc. Roy. Med. & Chir. Soc. 69: 493, 1886. (b) Tendlau, B.: Ueber angeborene und erworbene Atrophia cutis idiopathica, Virchows Arch. f. path. Anat. 167: 465, 1902. (c) Kaalund-Jorgensen, O., and Christensen, J. F.: Congenital Ectodermal Dysplasia of Anidrotic Type, Acta dermat.-venereol. 22: 1, 1941. (d) Upshaw, B. Y., and Montgomery, H.: Hereditary Anhidrotic Ectodermal Dysplasia: A Clinical and Pathologic Study, Arch. Dermat. & Syph. 60: 1170 (Dec.) 1949.
2. Whyte, G. D.: Congenital Absence of Breast, Lancet 2: 1249, 1904. Schneller, E. W.: Congenital Amastia, M. Rec. 53: 282, 1898. Viégas, A. P.: Amastia referencia de un caso, Brasil-med. 62: 201, 1948. Simard, René: Sur un cas d'amastie, Laval méd. 13: 687, 1948. Bertone, C.: Amastia unilaterale e deformità di una mano nello stesso soggetto, Rinasc. Med. 7: 548, 1930. Louria, H. W.: A Case of Unilateral Amastia, Am. J. Obst. 8: 364, 1924. Putzu Doneddu, F.: Un caso di amastia monolaterale, Arch. ostet. e ginec. 2 Ser. 21: 1, 1934. Lutaud, P.: Sur un cas d'amastie et brachydactylie, Arch. gén. de méd. 467, 1910. Gilly, E.: Absence complète de mamelles chez une femme mère: atrophie du membre supérieur droit, Courier méd. 32: 27, 1882. Paull, F.: Total Absence of the Left Mammary Gland, from Nondevelopment, Lancet 1: 648, 1862.

ss of the skin from lack of sebaceous glands. Obviously, there is no curative treatment, but it is important that such cases be diagnosed early and the heat regulation carefully watched by nurses or parents of the patient. As the child grows, he should be taught to watch his own heat regulation by avoiding hot foods and beverages in excess and strenuous exercise in a hot environment. In the case reported by Upshaw and Montgomery¹⁰ the patient was able to obtain gainful employment as a life-guard.



Fig. 1.—Patient in case reported, showing absence of nipples, saddle nose, prominent frontal bossing, thick, protruding lips, and lanugo fuzz.

The lack of sebaceous gland activity interdicts the usual use of soap and water. One of the superfatted soaps may be tolerated, if it is used in small amounts, or possibly one of the soap substitutes, such as oily pHisoderm® or a surface-acting detergent (terjolate®), may be suitable for cleansing. Further, the regular use of some bland oil, such as olive oil, baby oil, theobroma oil (cocoa butter), "nivea" skin oil (cholesterolized petrolatum in a water emulsion with eucerite), will keep the skin lubricated and help to prevent dryness, scaling, and fissuring.

Patients who have dental aplasia, as the patient in this case, should have early dental care. The consensus of the dentists I have consulted about this case is that complete dentures should be made as soon as it is possible to get the necessary cooperation of the patient. In the case re-

ported by Israel,⁵ full dentures were made for a child aged 4 to replace lost and infected deciduous teeth and roots; these apparently were completely satisfactory and were to be removed as the permanent teeth erupted. McBride⁶ advises the use of dentures in young children where they are indicated; he records the use of partial dentures in a child aged 4 and a full upper denture in a child aged 5. Full dentures were made by Bray⁷ for an edentulous child 13 years of age.

SUMMARY

The case of a Negro boy with congenital absence of nipples and breasts as a part of congenital ectodermal defect, further characterized by alopecia, dry, scaly skin, saddle nose, and complete absence of teeth, is reported. Comparison of the reported cases of such defect is made

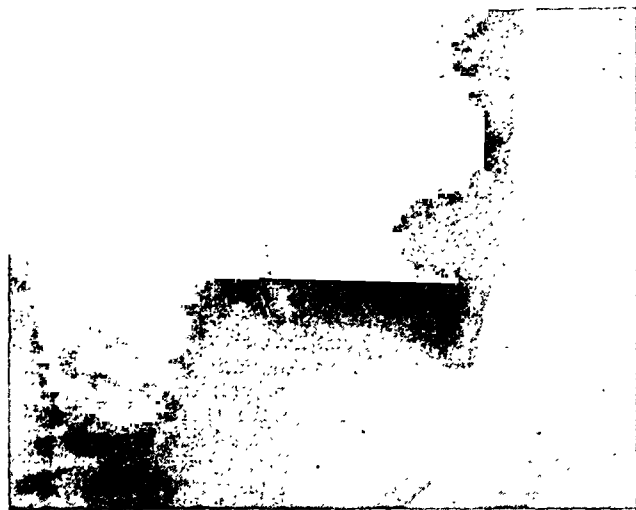


Fig. 2.—Head of patient in case reported, showing absence of teeth.

in tabular form. Suggestions for symptomatic management of patients with ectodermal defect, particularly to regulate body temperature and lubricate the skin, are given.

Columbia Medical Building, 1835 Eye St., N. W.

3. Wylie, W.: Case of Entire Absence of Both Mammæ in a Female Aged 21 Years, *Brit. M. J.* 2: 235, 1888. Batchelor, H. T.: Absence of Mammæ in a Woman, *ibid.* 2: 876, 1888. Glos, J.: Bilateral Amazia with Malformation of Extremities, *Časop. lékař. česk.* 71: 865, 1932. Ray, D. S.: Complete Absence of Breast in a Female, *St. Barth. Hosp. J.* 27: 158, 1919-1920. Liebenam, L.: Zwillingspathologische Untersuchungen aus dem Gebiet der Anomalien der Körperform. Partieller Riesenwuchs. Angeborener Pectoralisdefekt. Dysostosis cleidocranialis. Dysostosis cranio-facialis, *Ztschr. f. menschl. Vererb. u. Konstitutionslehre* 22: 373, 1938.

4. Owen, R.: Personal communication to the author.

5. Israel, W.: Dental Foci of Infection and Full Dentures for Children, *J. Southern California State Dent. A.* 16: 27, 1949.

6. McBride, W. C.: *Juvenile Dentistry*, Philadelphia, Lea & Febiger, 1945.

7. Bray, C., cited by McBride.⁶

Carcinoma of the Breast.—Carcinomas still limited to the confines of the breast are usually clinically indistinguishable from benign tumors, hence their clinical diagnosis is for all practical purposes the diagnosis of dominant lump. A dominant lump is one which varies from anything else felt in the breasts in size, consistency and differentiation from surrounding tissue. Between one third and one half of all such lumps are carcinoma. . . . —Louis P. River, M.D.; Joseph Silverstein, M.D., and Eugene F. Dolehide, M.D., *Carcinoma of the Breast, Symptoms and Diagnosis, The Journal of the Iowa State Medical Society*, December, 1951.

COUNCIL ON PHYSICAL MEDICINE AND REHABILITATION

The Council on Physical Medicine and Rehabilitation has authorized publication of the following report.

RALPH E. DE FOREST, M.D., *Secretary.*

PRESENT STATUS OF USE OF ULTRASONIC ENERGY IN PHYSICAL MEDICINE

The study of ultrasonic energy as a separate science began only a little more than 30 years ago, when high frequency acoustic vibrations were first employed for underwater communication. (This led to the development of "sonar" during World War II.) Since these studies began, several thousand articles on various applications of ultrasonic energy have been published and within the last few years hundreds of articles have been written concerning the medical applications of ultrasonic energy. Most of the articles on the medical employment of ultrasonic energy have been published in Europe, particularly in Germany and Austria, and until recently American physicians have shown little interest in this field. There has been an unfortunate exploitation of devices for ultrasonic therapy in Europe just as there was an exploitation of short wave diathermy devices about 15 years ago.

About 1935 the European medical literature, particularly the German and Austrian, was filled with exaggerated and uncritical claims concerning the value of short wave diathermy in a wide variety of diseases. Claims were made that short wave diathermy would be of value in the treatment of malignancy and it was also contended that these short wave electrical radiations had a number of effects other than those attributable to heating of tissues. Soon European short wave diathermy machines were being imported into the United States in large numbers and American manufacturers began producing them in even larger quantities. It took several years for careful medical investigators here and abroad to overcome this early exploitation of short wave diathermy, to define its limitations and to indicate its proper sphere of usefulness in medicine.

Now history is repeating itself with regard to the employment of ultrasonic energy. These ultrasonic devices are being exploited in Europe; exaggerated claims concerning their value in a wide variety of diseases are being made. It has been claimed by certain German physicians that ultrasonic energy is of value in the treatment of malignancy and they are also claiming mysterious effects other than those attributable to heating of tissues. Importations are now being made from Europe, and American manufacturers also are starting to make ultrasonic apparatus for use in medicine.

If ultrasonic energy is employed properly by skilled physicians and not used indiscriminately as a "cure-all," it offers promise of becoming a valuable new therapeutic and diagnostic agent. Therefore, it is important for American physicians to familiarize themselves with these ultrasonic machines, to examine critically the evidence concerning their possible diagnostic or therapeutic usefulness, and to determine promptly the limitations and dangers of ultrasonic therapy. Already it is apparent

This report is a summary of work performed by the following investigators of the Mayo Clinic and Mayo Foundation, Rochester, Minn.: Frank H. Krusen, M.D., Section of Physical Medicine and Rehabilitation; J. F. Herrick, Ph.D., Carl F. Schlotthauer, D.V.M., and Khalil G. Wakim, M.D., Ph.D., Division of Experimental Medicine; Warren A. Bennett, M.D., Section of Pathologic Anatomy, Joseph M. Janes, M.D., Section of Orthopedic Surgery; Edward H. Lambert, M.D., Ph.D., Section of Physiology; and Paul A. Nelson, M.D., Thomas P. Anderson, M.D., Ralph E. De Forest, M.D., and Walter J. Treanor, M.B., Fellows in Physical Medicine and Rehabilitation.

1. Nelson, P. A.; Herrick, J. F., and Krusen, F. H.: Ultrasonics in Medicine, *Arch. Phys. Med.* 31: 6-19 (Jan.) 1950.

2. Freundlich, H.; Söllner, K., and Rogowski, F.: Einige biologische Wirkungen von Ultraschallwellen, *Klin. Wchnschr.* 11: 1512-1513 (Sept.) 1932.

3. Pohlman, Reimar: Die Ultraschalltherapie: Quantitative Angaben zu ihrem Wirkungsmechanismus, *Deutsche med. Wchnschr.* 73: 373-377 (Sept. 3) 1948.

that the therapeutic application of ultrasonic energy may cause damage of an irreversible nature to certain tissues of the human body and that overdoses of ultrasonic energy are potentially dangerous. The margin of safety is much less with ultrasonic diathermy than with short wave diathermy.

ULTRASONIC APPARATUS

Commonly, ultrasonic vibrations are produced by using piezo-electric crystal. Certain crystals such as quartz will come electrically charged on opposite surfaces when they are subjected to mechanical pressure. This property is called "piezo-electric effect." The reverse effect also occurs, and a crystal will undergo mechanical vibration when opposite surfaces are subjected to an alternating electric field. It is comparatively easy to construct a piezo-electric transducer which converts electrical oscillations into mechanical vibrations which, in turn, produce sound waves. Such vibrations can be transmitted through a "sound head" to the surface of the body which is to be treated.

Unlike electromagnetic vibrations, ultrasonic radiations do not pass through a vacuum but require a material medium for their propagation. These ultrasonic waves travel approximately four times as fast in liquids, and up to twenty times as fast in solids, as they travel in air. High frequency sound waves travel in straight lines, are completely reflected at the interface between two mediums if the critical angle is exceeded, and exhibit interference phenomena and are refracted. A particle

TABLE 1.—Diseases Treated and Results Obtained by Ultrasonic Therapy as Presented by Two European Physicians*

Diagnosis	Cases	Results of Treatment, % †			
		++	+	0	—
Herpes zoster.....	51	55.0	19.5	23.5	—
Intercostal neuralgia...	128	58.6	22.7	17.1	—
Scleritis	1,508	62.0	22.6	10.3	0.5
Lumbago	213	67.7	18.2	4.7	—
Multiple sclerosis.....	106	2.8	42.5	49.1	2.8
Myalgia	99	39.5	49.5	5.0	1.0
Neuralgia	852	60.2	21.5	10.1	0.6
Periarthritis (humero-scapular)	177	35.5	43.0	15.2	1.1
Spondylitis (deforming) ..	273	36.6	49.5	9.1	2.2
Trigeminal neuralgia...	128	18.0	32.8	40.7	3.9

* From Matthes, K. and Rech, W.: *Der Ultraschall in der Medizin*, S. Hirzel Verlag, 1949, 485 pp.

† Result best = ++; result next best = +; no benefit = 0; condition worse = —; result questionable = ?.

the field is forced to vibrate through 800,000 cycles per second yet it is not displaced from its position of rest by more than one-hundred thousandth of a centimeter.

EFFECTS OF ULTRASONIC RADIATION

Space does not permit a description of the mechanical, thermal, chemical, biologic and physiologic effects of ultrasonic energy but Nelson, Herrick, and Krusen¹ have described some of these effects elsewhere.

An ultrasonic wave passing through a liquid alternately compresses and separates its component particles and with enough intensity the disruptive forces exceed the intermolecular bonds and the medium is actually split apart. This phenomenon which involves not only the formation of cavities but also the sudden collapse, is called "cavitation."

Freundlich, Söllner, and Rogowski² concluded that marrow could be strongly heated by ultrasonic radiation; therefore, they expressed the belief that the therapeutic possibilities of ultrasonic diathermy merited further study. Many European clinicians have mentioned an "analgesic effect" of ultrasonic radiation.

In Table 1 are listed a number of diseases in which ultrasonic therapy has been employed by European physicians. It will be noted that the largest number of cases treated included sciatica and neuralgia; also that a high percentage of beneficial results was reported.

European physicians, led by Pohlman,³ have concluded that an intensity of ultrasonic radiation of 2 to 5 watts per square centimeter, which produced erythema without edema, is the correct dose for treatment. A frequency of 800,000 cycles per second appears to be most satisfactory for therapy. This frequency we have used in our experiments.

On the completion of our original survey, three of us, Nelson, Herrick, and Krusen,¹ concluded that, despite enthusiastic claims of some European investigators, enough was not known concerning the physiologic effects of ultrasonic energy to warrant its use in treatment of any disease of man. Nevertheless, we concluded that the diagnostic and therapeutic possibilities of ultrasonic energy merited further careful scientific evaluation. Since then, we have sought further evaluation by suitable labo-

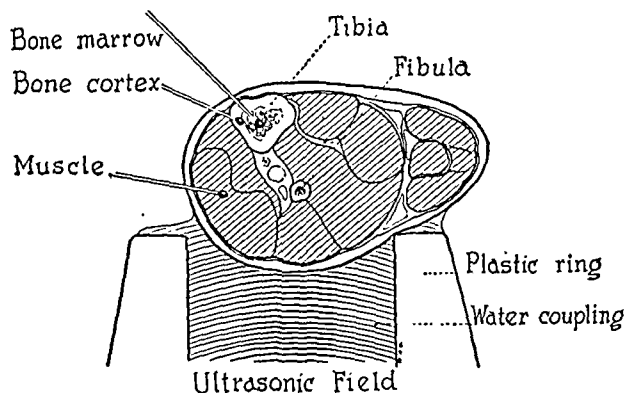


Fig. 1.—Cross section showing placement of thermistors in the hind leg of an anesthetized dog for measurement of the heating effects of ultrasonic energy on bone marrow, bone and muscle.

ratory studies on living animals. First, mindful of the report of Freundlich and his associates,² we asked ourselves the following questions:

What relative heating can be produced by ultrasonic radiation in living tissues such as bone marrow, bone cortex and muscle? Might ultrasonic radiation prove to be a useful form of medical diathermy? In attempting to answer these questions, three of us (Nelson, Herrick, and Krusen³) used a small, efficient ultrasonic generator, made by the Central Research Laboratories, and producing a maximal output of 15 watts. The area of the crystal used in this apparatus is approximately 5 sq. cm. We also obtained from Germany a Siemens "Sonostat," which delivered up to 60 watts of ultrasonic energy. In this device a piezo-electric crystal with an area of 10 sq. cm. is mounted in a grounded metal unit, which is called the appli-

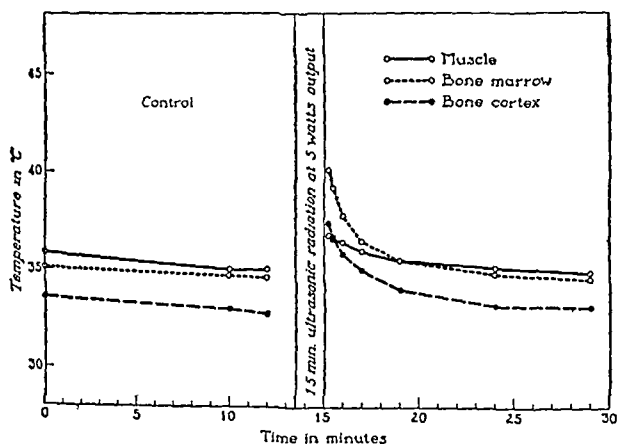


Fig. 2.—Temperatures produced by the application of ultrasonic energy to the lateral surface of the hind leg of an anesthetized dog. Data obtained in a typical run in which an exposure was made for 1.5 minutes at an output of 5 watts.

cator or "sound head," in such a way that the mechanical vibrations (ultrasonic waves) are conducted through a metal diaphragm.

Temperatures of bone marrow, bone cortex and muscle were measured with thermistors or by thermocouples. Figure 1 shows how the thermistors were placed in the bone marrow, bone cortex, and muscle of the hind leg of an anesthetized dog; Figure 2 shows a typical observation in which there was a

marked increase in the temperature of bone marrow when ultrasonic radiation was applied to the lateral surface of the dog's hind leg for one and one-half minutes at an output of 5 watts.

Table 2 shows the marked rises in temperature produced in bone marrow and bone cortex in only one and one-half minutes.

It will be noted that in these anesthetized dogs, if the wattage was increased from 5 to 10, the rise in temperature nearly doubled. After only one and one-half minutes of ultrasonic radiation at an output of 5 watts, rises of temperature of bone cortex and bone marrow were slightly greater than those obtained after 30 minutes of microwave radiation at an output of 65 watts. No observable gross damage to superficial tissues was noted following either microwave or ultrasonic radiation.

It was concluded that ultrasonic radiation can produce sharply localized heating of living tissues and can cause selective heating of bone cortex and bone marrow as does no other source of energy used thus far for medical diathermy, and further that if ultrasonic diathermy is administered clinically, a wide margin of safety with regard to dosage is necessary because of unexpected variations which frequently arise.

After completing this study, we next asked ourselves the question:

What are the effects of ultrasonic energy on the nervous system? To answer this question, Anderson, Wakim, Herrick, Bennett, and Krusen⁵ initiated studies on the lower part of the

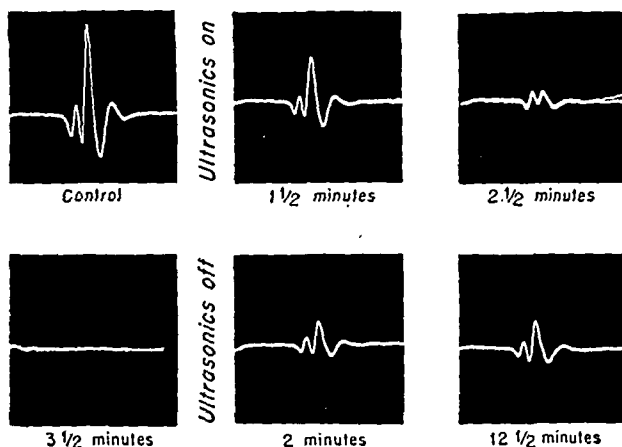


Fig. 3.—Effect of application of ultrasonic energy on the action potential of the sciatic nerve.

spinal cord and on peripheral nerves of living dogs. Clinical observation of paralysis and observation of alteration of action potentials of nerves were made. Temperatures produced by ultrasonic energy were studied and histopathologic changes in the nerve resulting from ultrasonics were also reported. Maximal doses were employed.

Studies of the effect of application of ultrasonic energy on action potentials were particularly interesting. Figure 3 shows the reduction to zero (complete block), such as occurred in 8 of 12 dogs within 10 minutes or less (in this case within 3 1/2 minutes) and the partial recovery thereafter. It was then found that the action potential of the sciatic nerve was decreased by direct heating in a strikingly similar manner.

The range of temperature (measured in the sheath of the sciatic nerve) at which the action potential becomes decreased was found to be narrow, i. e., between 48 and 52 C. If the action potential was only partially decreased recovery usually was complete, whereas if the action potential was completely flattened, there was usually only partial or no recovery.

Marked destruction occurred in every dog which exhibited paralysis following application of ultrasonic energy over the

4. Nelson, P. A.; Herrick, J. F., and Krusen, F. H.: Temperatures Produced in Bone Marrow, Bone, and Adjacent Tissues by Ultrasonic Diathermy: An Experimental Study, *Arch. Phys. Med.* 31: 687-695 (Nov.) 1950.

5. Anderson, T. P., and Krusen, F. H.: An Experimental Study of the Effects of Ultrasonic Energy on the Action Potential of the Sciatic Nerve and Peripheral Nerves, *Arch. Phys. Med.* 32: 687-695 (Nov.) 1951.

spinal cord. Figure 4 shows the severe necrosis and marked gross pathologic changes found in one such animal. Figure 5 is a photomicrograph showing normal muscle surrounding a nerve in which marked degenerative changes have been produced by local application of ultrasonic radiation.

On completion of these studies we concluded that ultrasonic energy applied in maximal doses over the lower vertebrae of dogs resulted in paralysis of the hind legs and tail. Furthermore,

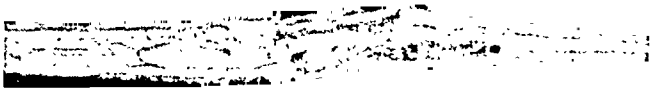


Fig. 4.—Gross appearance of the spinal cord of a dog which was exposed to ultrasonic energy in a dosage of 5 watts per square centimeter applied for 10 minutes over the upper lumbar vertebrae. Complete paralysis of the legs and tail ensued. At necropsy severe necrosis and other gross pathologic changes were found

ultrasonic energy in the amount of 3.0 to 5.8 watts per square centimeter, applied to the mid-thigh, resulted in complete blocking of, or at least 50% decrease in, the action potential of the intact sciatic nerve in 60% of the dogs studied. Recovery, as indicated by the action potential, was usually complete when the action potential had been only partially decreased by the



Fig. 5.—Photomicrograph of section of small nerve in a superficial muscle of a rat three weeks after direct exposure to ultrasonic energy. Although the nerve exhibited the unusual regular pattern of myelin degeneration which was commonly produced by ultrasonic energy, no evidence of change could be seen in the muscle surrounding the nerve.

ultrasonic energy but recovery was generally incomplete when the amplitude of the action potential had been completely flattened. Direct heating produced a strikingly similar effect on

the action potentials. Ultrasonic energy had much greater destructive effect on the spinal cord than on the sciatic nerve.

Following a lead developed in this study on nerves, we asked ourselves another question:

What are the relative effects of heat and ultrasound on conduction of nerves? (Are the effects of ultrasound on peripheral nerves owing entirely to heat or do the effects differ from those caused by conductive heating?) Treanor, Lambert, Herrick, and Krusen⁶ continued this study by irradiating the sciatic nerve of a bullfrog between stimulating and pick-up electrodes at a level of 4 watts per square centimeter. The effect is illustrated in Figure 6. The upper curve shows the temperature of the nerve bath and below are the sound curves indicating the amplitude of the "A" and "B" spikes of the nerve action potential. The periods of irradiation with ultrasound are shown by the upper bar. The periods of cooling of the bath by circulation of fluid through it are shown by the lower bar.

TABLE 2.—Results Obtained on Experimental Heating of Tissues of Hind Legs of Anesthetized Dogs*

Wattage	Runs	Tissue	Average Rise in Temperature, C.
5	13	Bone marrow.....	5.39
		Bone cortex.....	5.92
		Muscle.....	1.12
10	9	Bone marrow.....	10.29
		Bone cortex.....	10.50
		Muscle.....	2.21

* Data obtained 15 seconds after exposure for 1.5 minutes to ultrasonic radiation. (Note that the temperature of bone marrow and bone cortex were increased in only 1.5 minutes to high levels and that when the wattage was increased from 5 to 10, these increases were nearly doubled.)

TABLE 3.—Comparison of Effects of Direct Heating (Thermode) and Ultrasonic Energy on Production of Conduction Block in Various Fiber Groups of Sciatic Nerve

		Fiber Group *				
		A			B	C
Thermode	°C.	45.4 ± 0.1	45.6 ± 0.1	45.6 ± 0.3	43.5 ± 0.1	45.1 ± 0.1
	n	15	12	10	19	12
Ultrasound	°C.	45.5 ± 0.3	45.5 ± 0.3	45.7 ± 0.3	43.4 ± 0.2	44.8 ± 0.2
	n	9	8	7	18	11
Difference †		— 0.1 ± 0.3	0.1 ± 0.3	— 0.1 ± 0.4	0.1 ± 0.2	0.3 ± 0.2

* Sciatic nerve of *Rana catesbeiana*.
† Mean and its standard error.
‡ Note that the differences are negligible.
N—Number of experiments.

When the temperature of the bath was allowed to rise by stopping the circulation of the coolant, decrease of the action potential occurred, indicating a block of conduction in some fibers. When the temperature was maintained at a low level, there was no apparent effect of the ultrasound over long periods of time. Note also that there was some evidence of a differential effect on "A" and "B" fiber groups. It seemed desirable to determine whether the effects of ultrasound on peripheral nerves were owing entirely to a rise in temperature of the nerve or whether the effects of ultrasound occur at lower temperatures than those of heat alone. Experiments indicated that ultrasound of intensities and frequencies employed in physical medicine at the present time has no effects on conduction in peripheral nerves other than those produced by the rise of temperature.

The data which are summarized in Table 3 indicated that the temperature at which complete block of fiber groups occurred was essentially the same whether heating was produced by thermode or by ultrasound. This warrants the conclusion that ultrasound of intensities and frequencies employed in physical medicine probably has no effects on conduction in peripheral nerve other than those produced by the rise of temperature. It is of interest also that the differential effects of heat on the nerve do not suggest an explanation of the so-called analgesic effects of heat.

6. Treanor, W. J.; Lambert, E. H.; Herrick, J. F., and Krusen, F. H.: Comparative Study of the Effects of Heat and Ultrasound on Nerve Conduction, unpublished data.

Next we asked ourselves the following question:

What are the effects of ultrasound on the growing ends of long bones? To answer this question, De Forest, Janes, Herrick, and Krusen⁷ studied the effect of ultrasonic energy on the hind legs of dogs which were 4 to 6 months old. The dogs in these new experiments were anesthetized, and the sound head was kept moving to minimize the effect of standing waves and to distribute the radiation better throughout the bone. The medial surface of the leg over the upper tibial epiphysal region was placed on a plastic applicator filled with degassed water from a reservoir bottle. This water served as the coupling medium between the sound head and the animal's leg.

Figure 7 shows the result when eleven ultrasonic applications of 10 watts for five minutes were given to one young dog. Eleven weeks after the last application, the roentgenogram was made. It shows obliteration of the lateral half of the upper tibial epiphysal line, destruction of the medial part of the medial tibial plateau, erosion of the surface of the medial condyle of the femur, and partial obliteration of the lower femoral epiphysal line.

Four ultrasonic applications of 10 watts for 10 minutes were given to another young dog, and two weeks later a fifth application was made (Fig. 8). Nine weeks and three days after this last application there was obliteration of the upper tibial epiphysal line in its lateral half, destruction with partial resorption of the upper tibial epiphysal, rarefaction in the condyles of the femur, obliteration of the lower femoral epiphysal line,

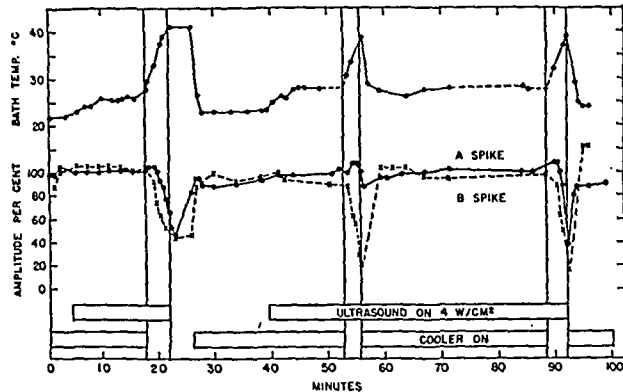


Fig. 6.—Effect on the "A" and "B" spikes of the action potential of the sciatic nerve produced by varying the temperature of a bath in which the nerve was placed and by applying ultrasonic energy to the nerve. (See the text for further explanation.)

dislocation of the knee joint, and swelling of the soft tissues.

It was obvious that ultrasound is very destructive to the growing bones of the dog when administered in the manner and doses described. Until safe dosages are determined through further investigation, ultrasonic therapy should not be applied to growing bones.

Having completed these studies, we asked ourselves another question:

What are the histopathologic effects of ultrasound on tumors? Bennett, Herrick, Schlotthauer, and Krusen⁸ conducted these studies. First, we studied the effect on a transmissible lymphosarcoma originated by Carl Olsen, Jr. Figure 9 shows a cross section made by freezing an entire chicken and sawing across it, thus giving this picture of the viscera and the treated tumor. This tumor had been injected into the breast five days before treatment. This chicken was treated for 30 minutes at 15 watts on two occasions. The necrosis of the skin and underlying tumor is well outlined. The solid mass infiltrating the muscle is the remaining portion of the tumor.

When a transmissible glioma of the ependymoma type, in a mouse, was treated for 75 seconds with 15 watts, there was a large amount of necrosis, but still much viable tumor remained.

When a Walker carcinoma in a rat was treated with 20 watts for 10 minutes, there was focal necrosis of skin, muscle, and tumor, and when a spontaneous squamous cell carcinoma of a dog was treated with ultrasound for 30 minutes at 15 watts, there was necrosis of the tumor but there was also much viable tumor remaining.

When a plasma cell myeloma of a dog was treated for 30 minutes with 15 watts, there was superficial necrosis but little or no effect on the tumor.



Fig. 7.—Roentgenogram showing the damage done to the bones of the hind leg of a young dog following 11 applications of ultrasonic energy of 10 watts for five minutes each. (See the text for further explanation.)



Fig. 8a and b.—Roentgenograms showing the damage done to the bones of the hind leg of a young dog following five applications of ultrasonic energy of 10 watts for 10 minutes each. (See the text for further explanation.)

It was concluded that among the tumors treated there was no demonstrable selective action. There was as much destruction of

7. De Forest, R. E.; Janes, J. M.; Herrick, J. F., and Krusen, F. H.: The Effects of Ultrasound on the Growing Ends of Long Bones; a Preliminary Report, unpublished data.

8. Bennett, W. A.; Herrick, J. F.; Schlotthauer, C. F., and Krusen, F. H.: Histopathology of Tissues Exposed to Ultrasonic Energy, published data.

normal tissues as there was of the tumor. It was possible to cause necrosis at will in the tumors but never possible to destroy them completely.

We then asked ourselves one final question:

What are the histopathologic effects of ultrasound on normal tissues? When normal chicken liver was exposed to a maximal



Fig. 9.—Cross section of a chicken showing the gross appearance following two applications of ultrasonic energy of 15 watts for 30 minutes. The energy was applied to skin over a transmissible lymphosarcoma of the breast. Evidence of necrosis of the skin and of part of the tumor can be seen but much viable tumor remains. (See the text for further explanation.)

dose of ultrasonic energy, there was necrosis immediately beneath the breastbone. The energy had penetrated the bony structure. When the skin of a dog was examined microscopically three days after an application of 25 watts for four minutes, there was ulceration of the epidermis, with necrosis of all elements including the muscle.

We found that there was a selective destruction of hair follicles just as there was selective destruction of nerve tissue. Figure 10 shows, for comparison, normal dog testes. Figure 11 shows dog testes following one treatment of 15 watts for thirty minutes. There is marked destruction of all cells except the basal elements in the seminiferous tubules. When the intestine of a rat was examined one hour after a treatment with 20 watts for 10 minutes, it was noted that there was diffuse necrosis throughout the thickness of the wall of the intestine. This occurred at the point of a gas bubble in the intestine, which acted as a barrier, with reflection of the ultrasonic energy so that this part of the intestine was severely damaged by the extra exposure caused by the combination of the original and the reflected radiation.

The skin exhibited an initial reaction of hyperemia followed by edema of the epidermis and dermis and the necrosis and formation of blebs. This necrosis often extended into the muscle.

The changes in the muscles included edema and interstitial hemorrhage followed by degeneration of the fibers, increase in sarcolemma cells, and a hemorrhagic appearance of the fibers. Finally, collapse of the muscle fibers was noted. If this collapse did not occur, then there was calcification of the degenerated fibers.

Necrosis of the spinal cord was marked throughout its entire thickness. There was extensive destruction of myelin and of all the elements of the cord. This resulted in complete paralysis, with marked necrosis and early phagocytic reaction.

The nerve fibers showed myelin degeneration, which often was patchy. In other areas it was rather diffuse. Accompanying the myelin destruction there were swelling and lobulation of the axons. Nerves may be markedly involved in the center of masses of muscle which show little or no change.

In mature bone there was fragmentation of the trabeculae with hemorrhage and destruction of the marrow. In immature bone there was erratic growth of cartilage, which was irregularly ossified. The marrow also was markedly destroyed.

It was concluded that ultrasonic energy can produce markedly destructive reactions in tissues, occurring at the point of application of the ultrasonic energy, throughout the pathway of the radiation through the tissues, or at the point of exit. The intensity of the destructive effects varies according to the type and density of the tissues or according to the presence or absence of fascial barriers. The reactions obtained in various animals were similar and varied not with the animal but with the intensity and duration of the treatment.

GENERAL CONCLUSIONS AND COMMENT

Throughout all of these studies maximal dosages usually were employed. Yet, except in one study, the dosages did not exceed even half those available on one of the machines which is commonly employed by physicians. The maximal dosage we employed (except in a few instances) was 25 watts for 30 minutes. The machine is capable of providing 60 watts for indefinite periods of time. It is apparent that such a machine, employed at maximal dosages, can severely damage many types of tissues; the spinal cord, peripheral nerves, testes, growing bones, and hair follicles appear to be particularly susceptible to damage.



Fig. 10.—Photomicrograph of section of normal testis of a dog. (For comparison with Figure 11.)

The danger of intensification of dosage by reflection must always be considered. The effects of ultrasonic energy on living tissues appear to be chiefly those of heating.

Having explored, rather fully, the effects of maximal dosages of ultrasonic energy on living animals, we now propose to investigate the effects of smaller dosages and to attempt to ascer-

tain what the optimal dosages, if any, may be. It is certain that ultrasonic energy is a potent destructive agent which may be extremely dangerous if employed indiscriminately by unskilled persons. Nevertheless, continued laboratory investigations of the therapeutic and diagnostic possibilities of this new and potent physical agent assuredly are justified.



Fig. 11.—Photomicrograph of section of testis of a dog following one exposure to ultrasonic energy of 15 watts for 30 minutes. (Note the marked destruction of all cells except the basal elements of the seminiferous tubules.)

The medical diagnostic possibilities of ultrasonic energy are intriguing. Ludwig and Struthers⁹ at the Naval Medical Research Center in Bethesda, Md., have developed a technique for locating nonradiopaque gallstones and foreign bodies at operation by ultrasonic means. Wild¹⁰ at the University of Minnesota School of Medicine has devised a method of measuring the thickness of the intestinal mucosa by ultrasonic methods and Hueter and Bolt,¹¹ working at the Massachusetts Institute of Technology, have developed a procedure for performing ventriculography by ultrasonic means (sonography).

Many potent therapeutic agents are dangerous in overdoses. When no anesthesia is employed, pain will serve as a protective mechanism for prevention of overheating of tissues. With proper dosage, ultrasonic diathermy may produce valuable selective heating effects not previously obtainable. It is recognized that ultrasound may produce effects, other than thermal ones, on the tissues. However, the effects are obviously chiefly those of heating and there is no need for ultrasound to produce other mysterious effects for it to be of value in therapy.

Although many hundreds of patients have been treated with ultrasound, particularly in Europe, apparently without harmful effects, it is believed that physicians should await further cautious study of ultrasonic therapy before using it indiscriminately in clinical practice.

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COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, M.D., Secretary.

Acet-Dia-Mer-Sulfonamides (See THE JOURNAL, Oct. 20, 1951, page 759).

Suspension Dorsulfas: 473 cc. bottles. A suspension containing 33 mg. each of sulfacetamide, sulfadiazine, and sulfamerazine in each cubic centimeter. Smith-Dorsey Company, Lincoln, Neb.

Tablets Dorsulfas: 0.5 gm. Each tablet contains 0.167 gm. each of sulfacetamide, sulfadiazine, and sulfamerazine. Smith-Dorsey Company, Lincoln, Neb.

Aminophylline-U.S.P. (See New and Nonofficial Remedies 1951, page 299).

Tablets Aminophylline: 0.2 gm., enteric coated. Keith-Victor Pharmacal Company, St. Louis.

Caprylic Compound (See New and Nonofficial Remedies 1951, page 45).

Vaginal Creme Naprylate: 90 gm. tubes. A cream containing 0.1 gm. of sodium caprylate and 50 mg. of zinc caprylate in a water miscible base. Packaged with a plunger-type applicator. R. J. Strassenburgh Company, Rochester, N. Y.

Choline Dihydrogen Citrate (See New and Nonofficial Remedies 1951, page 411).

Tablets Choline Dihydrogen Citrate: 0.65 gm. Physicians' Drug & Supply Company, Philadelphia, Pa.

Diethylstilbestrol-U.S.P. (See New and Nonofficial Remedies 1951, page 340).

Tablets Diethylstilbestrol: 1 mg. and 5 mg. uncoated. 0.25 mg., 0.5 mg., 1 mg., and 5 mg. sugar coated. Chicago Pharmacal Company, Chicago.

Folic Acid-U.S.P. (See New and Nonofficial Remedies 1951, page 440).

Tablets Folic Acid: 5 mg. Physicians' Drug & Supply Company, Philadelphia.

Neostigmine Methylsulfate-U.S.P. (See New and Nonofficial Remedies 1951, page 184).

Solution Neostigmine Methylsulfate 1:2000: 1 cc. ampuls. E. S. Miller Laboratories, Inc., Los Angeles, Calif.

Paramethadione (See New and Nonofficial Remedies 1951, page 256).

Capsules Paradione: 0.15 gm. Abbott Laboratories, North Chicago, Ill.

Phenylephrine Hydrochloride-U.S.P. (See New and Nonofficial Remedies 1951, page 198).

Solution Neo-Synephrine Hydrochloride 0.5% (Intranasal): 30 cc. bottles. A buffered isotonic solution containing 0.5 gm. of phenylephrine hydrochloride in each cubic centimeter. Preserved with 0.02% methylparaben, 0.01% propylparaben, and 0.2% sodium bisulfite. Winthrop-Stearns, Inc., New York.

Sulfadiazine-U.S.P. (See New and Nonofficial Remedies 1951, page 96).

Tablets Sulfadiazine: 0.5 gm. Mallard, Inc., Detroit, Mich.

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AORTOGRAPHY

Reinaldo Dos Santos, a Portuguese urologist, reported in 1929 before the Surgical Society of Paris his technique of translumbar aortography and clinical experiences with this method of visualizing the abdominal aorta, its branches, and the arteries of the lower extremities. Dos Santos performed 300 abdominal aortographies without an accident. He later reported one instance of bleeding in 1,500 cases. In a recent review of the experiences with this method at the Presbyterian Hospital in New York City, Deterling¹ reports no mortality in 100 aortographies. The needle hole readily seals itself because of the elasticity and thickness of the arterial wall. No hemorrhage was observed. Puncture through an atheromatous plaque is but rarely a cause of complication. The morbidity was minimal following injection of organic iodides.

Wagner and Price² reported one fatality in their series of 50 abdominal aortographies. This was due to the needle entering the superior mesenteric artery, which then received all of the iodide solution intended for the abdominal aorta, with resulting mesenteric thrombosis. Nelson³ was first in this country to perform translumbar aortography. He had no fatalities in more than 100 cases. Another urologist, Doss,⁴ stated that one of the fundamental requirements for obtaining a satisfactory abdominal arteriogram is adequate concentration of the radiopaque medium within the artery at the instant the roentgenographic exposure is made. He designed a special apparatus capable of exerting 3 atmospheres (45 lb.) of pressure on the fluid to be injected. He confirmed Nelson's observation of obtaining satisfactory "renograms."

Such a renogram made possible recognition of a number of pathological processes within the kidney, such as renal agenesis, renal duplication, renal ectopia, retroperitoneal tumors, renal neoplasia, and cysts of the kidney.

Wagner and his co-workers⁵ described a slightly modified technique of abdominal arteriography in which they used a 15 cm., no. 18 gage needle and a hand syringe for injection. Indications for abdominal aortography are aneurysm of the aorta, aortic occlusion, peripheral vascular disease, abdominal tumors, hypertension, and hydronephrosis. They felt that, although they had no untoward results in 26 instances, the method was not without potential dangers. It should therefore be employed as a diagnostic adjunct by carefully trained personnel only after simpler and standard studies have failed to yield sufficient information. Price and Wagner⁶ demonstrated a complete aortic block just below the origin of renal arteries in two patients. Diagnosis was made during life by direct translumbar aortic injection of radiopaque medium. Collateral blood supply in cases of obstruction of the abdominal aorta is mainly by anastomosis of the inferior with the superior epigastric arteries and by a paravertebral anastomosis of lumbar arteries. The most important anastomosis among the visceral arteries is that of the middle colic with the left colic, thus allowing the inferior mesenteric artery to receive blood from the superior mesenteric artery and preventing gangrene of the sigmoid.

Translumbar aortography, as developed by Dos Santos, has now been practiced in some 3,000 cases. The needle is inserted just below the 12th rib and 4 finger-breadths to the left of the spinal processes. The opaque medium must be nontoxic, nonirritating, rapidly excreted, and nonhemolyzing. Sodium iodide, which is customarily employed, can produce iodism and allergic reactions. Iodopyracet (diodrast®) in 70% solution does not produce so good a picture of the smaller arteries but is satisfactory. The method should not be used in the presence of severe liver damage, nephritis, uremia, or sensitivity to iodides. Deterling states that injection of 1,000 cc. of isotonic sodium chloride solution and of 500 mg. of vitamin C intravenously immediately after the procedure prevents iodism. The method can be used with the patient under local anesthesia or with thiopental sodium (pentothal®) intravenously for general anesthesia.

Castellanos and Pereiras⁷ introduced in 1937 the retrograde method of visualizing either the thoracic or the abdominal aorta. The thoracic aortography was accomplished through injection into the brachial artery. The abdominal aortography was performed by injecting the femoral artery under pressure. Somewhat later, Fariñas⁸ reported injecting the abdominal aorta by a method in which the femoral artery was exposed and 50 cc. of a 70% solution of iodopyracet was injected with a trocar within two and one-half and three seconds. The injection is made with a specially designed apparatus. In this country, Burford and Carson⁹ utilized the left common carotid artery for demonstration of the anomalies or disease of the aorta and its immediate branches. They considered the method safe, dependable, and effective in the diagnosis of questionable cases of patent ductus arteriosus, coarctation of the aorta, and aortic arch anomalies. Goodwin and his associates¹⁰ utilized a

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8. Fariñas, P. L.: Retrograde Abdominal Aortography: A Contribution to the Study of the Abdominal Aorta and Iliac Arteries, *Radiology* 47: 344-348 (Oct.) 1946.

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ureteral catheter, which was placed into the lateral circumflex branch of the profunda femoris artery and into the femoral artery up into the aorta. They felt, however, that the translumbar needle aortography is simpler, less hazardous, and should be the method of choice. Pearl and associates¹¹ passed a catheter into a peripheral artery and guided it under fluoroscopic control to the aorta and to many of its larger branches. They were able to demonstrate the coronary arteries.

The consensus is that translumbar needle aortography is safer and simpler than the retrograde catheter method. They are not regarded as routine diagnostic procedures but rather as diagnostic adjuncts in cases in which standard methods fail to reveal the lesion. Congenital anomalies of the heart, certain cardiovascular lesions, and lesions of the kidneys constitute the field in which the newer methods of arteriography will find their application.

LYSOZYME AND ULCERATIVE COLITIS

Since Meyer and his group,¹ in 1947, reported elevated fecal lysozyme concentrations in patients with ulcerative colitis, a number of studies of the possible role of lysozyme in the etiology of this disease have been reported. Recently, some investigators have cast doubt on the possibility that lysozyme may cause ulcerative colitis; but they emphasize the usefulness of the fecal lysozyme titer as an index of the degree of activity of the disease process.

Meyer's group² had previously observed that lysozyme was capable of removing the surface mucus from the stomach of a dog. Simultaneously they reported that in six patients lysozyme titers of gastric juice after vagectomy showed a mean fall of 44.4%, compared to preoperative levels, which suggests that lysozyme production is influenced at least in part by nervous control. They hypothesized that ulcerative colitis may be due to local overproduction of lysozyme followed by a necrotizing action on the mucosa by the indigenous bacterial flora. These workers subsequently produced ulceration of the stomach, small intestine, and colon in dogs by feeding lysozyme³ and later reported almost uniformly high lysozyme content of the stools and mucosa in patients with ulcerative colitis. They also noted a fall in the lysozyme titers with clinical improvement.⁴

Portis,⁵ recalling Meyer's hypothesis of the existence of a neural mechanism, suggested that increased emotional stimuli carried by the sacropelvic nerves may result in a high concentration of lysozyme in the colon leading to the loss of protective mucus. Grace and co-workers⁶ found that, in normal subjects and in subjects with diarrhea but without ulceration, transitory elevations in fecal lysozyme often occurred in association with emotional upsets. In patients with ulcerative colitis, on the other hand, marked and sustained elevations of lysozyme occurred. The high titers immediately preceded exacerbations of colitis.

Glass⁷ cast doubt on the etiological role of lysozyme when he reported that colonic mucus was not digested by lysozyme in vitro. He pointed out that the concentration of lysozyme used by Meyer to produce ulceration in the

dog is higher than might be encountered in human pathological processes. Glass infers from his studies that, whatever the consequences of increased lysozyme in ulcerative colitis, they do not include digestion of the colonic mucus.

According to Gray,⁸ prolonged inhibition of fecal lysozyme in six patients by oral administration of a detergent ("aerosol OT" [dioctyl sodium sulfosuccinate]) did not alter the course of the disease, which indicates that lysozyme does not play a significant role in the pathogenesis of ulcerative colitis. He reported that a profound decrease in fecal lysozyme, coincident with clinical improvement, occurred in all patients who responded to corticotropin (ACTH) therapy.⁹ Gray believes the fecal lysozyme titer correlates with the amount of functioning tissue and its ability to respond to injury. In the presence of sufficient functioning tissue, the titer serves as an index of the activity of the disease process. Gray suggests that the decrease in fecal lysozyme following corticotropin therapy may be due to an inhibitory effect of corticotropin on the tissue's response to injury. He cautions, however, that inhibition of fecal lysozyme by a detergent does not necessarily reflect inactivation of the enzyme within the mucosal cells. Moreover, while lysozyme may not digest intraluminal mucus, its mucolytic action on intracellular mucus is not known.

Sammons¹⁰ presented evidence indicating that the source of lysozyme in the feces in ulcerative colitis may be the pus cells. This would oppose the possibility of an etiological role. He found a second mucinase in the feces of patients with ulcerative colitis not present in normal persons, which, unlike lysozyme, does attack mucus. He suggests that this mucinase may play a part in the etiology of ulcerative colitis.

Lysozyme has not been generally accepted as a causative agent of ulcerative colitis. It is, however, being more widely studied as an index of the degree of activity of the disease process and as a measure of the available functioning colonic tissue. Further research in this field should produce results of much clinical importance.

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THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

During much of the first century of its life your American Medical Association was concerned primarily with purely scientific affairs. Socioeconomic pressures on medicine, however, began piling up during the depression and the war. They were accompanied by and, in part, caused by increasing governmental ventures into health and medical care. The government also wielded an indirect influence on American medicine as we had known it by great increases in taxation, which destroyed much of the private support for our hospitals and medical schools.

These socioeconomic pressures created new problems and duties for your national Association. It became necessary to establish new departments to deal with them. In 1943 the House of Delegates created one of the most important of these—the Council on Medical Service and Public Relations. Its purpose was to “study the effect of social and economic changes on the practice of medicine and to report these changes to the profession.”

This Council indeed has been a pioneering one. It has had to steer a path through turbulent and uncharted waters. Some of its early projects expanded so greatly and became so important that they were separated from the Council and set up as separate departments directly under the Board of Trustees. The two outstanding examples of this are the Washington Office and the Department of Public Relations.

Today the Council, known by the shortened title “Council on Medical Service,” works in seven major areas. It has a committee to conduct studies and develop long-range plans in each. The seven areas are (1) prepayment hospital and medical service, (2) relations with lay-sponsored voluntary health plans, (3) federal medical services, (4) extension of hospitals and other facilities, (5) maternal and child care, (6) indigent care, and (7) medical care for industrial workers. I shall be able to touch only briefly on the Council activities in these fields. To do justice to them, a President's Page would have to be written about each committee.

The Council's Committee on Prepayment Hospital and Medical Service studies and evaluates voluntary health insurance plans, both those written by private insurance carriers and those sponsored by medical societies. It accepts applications for the Council's Seal of Approval and grants it to those plans meeting Council standards. The Committee also studies ways and means of improving benefits under all types of voluntary health insurance.

With the growth in recent years of a number of lay-sponsored and lay-managed health insurance plans, the Council set up a special committee to establish criteria for evaluating such plans. This Committee maintains liaison with the managing groups and is encouraging them to establish high standards of health service.

The Committee on Federal Medical Services was originally called the Committee on Medical Care for Veterans, and its early work was confined to the study of the several medical programs of the Veterans Administration. Its work has now been broadened to include the study of all federal activities in the medical care field not covered by other A. M. A. Councils or committees. (For example, the Council on National Emergency Medical Service handles relations with the Civil Defense Administration and the Medical Services of the Armed Forces.)

One of the most active committees is that on the Extension of Hospitals and Other Facilities. It considers hospital-physician relationships and encourages state and county medical societies to set up liaison committees between hospitals and physicians. It follows progress made under the Hill-Burton Hospital Construction Act. It advises on the development of needed health centers, diagnostic clinics, and outpatient dispensaries. Quite naturally, one of its activities is to study the distribution of physicians and to attempt to improve the situation in areas short of doctors. Accordingly, it operates the A. M. A.'s National Placement Service, which serves communities needing a physician and physicians seeking a place to practice.

The Committee on Maternal and Child Care regularly reviews activities in that field. It reports its findings to the profession, and, from the information gathered, is developing suggested minimal programs for communities of various sizes. Because of the recent agitation in governmental circles for a revival of the Emergency Maternal and Infant Care program, the Committee is currently conducting a series of studies to determine whether an emergency program is necessary.

Another Committee that is currently conducting a series of studies is the Committee on Indigent Care. These studies, which have been under way for the past year, cover all the various types of indigent care programs in operation in the United States. From the findings the Committee hopes to determine trends in indigent care and will attempt to formulate some suggested programs. One trend that the Committee has noted is the increasing amount of public assistance medical care being rendered by local health departments. The Committee endeavors to determine the relationship of the private practitioner to

such programs as well as to all other indigent care plans.

Working closely with the Council on Industrial Health, the Committee on Medical Care for Industrial Workers reviews the scope of medical care programs now available to industrial workers. It also evaluates the status of physicians in industrial medical care programs. The Committee has given special attention to a study of cash sickness benefits legislation.

As is clear from the above description, much of the work of the Council on Medical Service is in the nature of surveys, studies, and evaluations. The material developed by its various committees is available to members of the A. M. A. who are faced with similar problems in their local communities. In addition to coordinating the activities of its Committees, the Council is concerned with many other problems and programs such as group practice, emergency medical call programs, health councils, temporary disability benefits, grievance committees, social insurance programs in foreign countries, local health units, multiphasic screening, and union health programs. Loan packets are available on these subjects as well as on some of the Committee activities. The Council can supply information on voluntary health insurance and on socialized medicine.

With socioeconomic problems ever present, we hope you will call upon your A. M. A.'s Council on Medical Service for the information it has available. It has been compiled as a service to members of the American Medical Association.

JOHN W. CLINE, M.D., San Francisco.



ORGANIZATION SECTION

FEDERAL MEDICAL LEGISLATION

Female Military Medical Officers

Senator Hunt of Wyoming introduced S. 2552, and Representative Durham of North Carolina introduced H. R. 6288. These bills are identical and would authorize the appointment of qualified women as physicians and specialists in the medical services of the Army, Navy, and Air Force. The bills would authorize the commissioning of women as officers to perform medical, dental, or medical service duties in the armed forces with equal rank and responsibility as now designated for male officers. These bills are similar to H. R. 4384 of the last Congress, which passed both the House and Senate. While these bills were being considered by a conference committee, the Congress adjourned, thus preventing their enactment.

STATE MEDICAL LEGISLATION

Arizona

Bills Introduced.—H. 156, proposes the creation of a state board of medical herbalists and defines a medical herbalist as a college graduate who holds a diploma from a recognized medical herbalist college, has studied anatomy, physiology, materia medica, toxicology, pharmacology, the metric system of weights and measures, diagnosis of diseases and herbal treatments for various diseases and malfunctioning conditions of the human body, and who deals exclusively in herbs, roots, barks and the compounding, preparation, and administration of the same as herbal remedies in the form of infusion, decoction, fermentation in substance, solid and fluid extracts, and tinctures and other natural forms. H. 161, proposes that no medicinal preparation or appliance having special utility for the prevention of venereal disease shall be sold except by an establishment holding a state license therefor issued by the state board of pharmacy except that the proposal would not apply to a duly licensed physician in the regular course of his practice. H. 162, proposes the creation of an Arizona board of medical technology which is defined to mean a science, art or technic of performing laboratory tests or examination on, or of, the blood, blood serum, feces, urine, sputum, exudates, transudates, organ contents or by-products thereof, from the human body, living or deceased, the results of which are used or interpreted by a practitioner licensed to engage in the practice of medicine. H. 168, to amend the law relating to naturopathy, proposes that approved colleges shall include in their course of study training in minor surgery, biochemistry, and phytotherapy in addition to subjects already covered by the law. The proposal would also add to the naturopathic act conditions under which it may be possible for licentiates to practice minor surgery after demonstrating proof of additional educational qualifications and passing a special examination.

Colorado

Bill Introduced.—H. 76, proposes the creation of a committee on mental hygiene to make a survey and study of mental health problems of the state.

Bill Enacted.—S. J. R. 12, was adopted Feb. 8, 1952, it creates a legislative committee to investigate the feasibility of establishing additional public facilities for the care of the aged either by enlargement of the Colorado State Hospital or by the establishment of one additional institution or several small institutions at various points throughout the state.

Kentucky

Bills Introduced.—H. 155, proposes that any person who has been engaged in the practice of medicine for forty years prior to the effective date of this act and who presents affidavits from two reputable licensed members of the medical profession who practice in the same general locality with him and know his professional qualifications to the effect that he is qualified to be a member of the medical profession shall be entitled to a license to practice medicine upon application to the state board of health. H. 172, proposes to require the department of health to establish and maintain services and facilities, including hospital schools, for the care and education of physically handicapped persons and to provide in connection therewith medical and nursing care. H. 174, proposes the creation of an alcoholic study commission to make a comprehensive study of the problem of alcoholism in the state, the existing methods and facilities for treatment, the present program of public education on alcoholism, and the present status of the laws of the state in regard to alcoholism. H. 280, proposes that no person engaged in any of the healing arts shall employ the title Doctor unless he actually has graduated and holds a Doctor degree from a school, college, university, or

institution authorized by its governing body to confer such degree. In such instances the person using the title Doctor must designate the particular Doctor degree which he holds. S. 93, proposes that no dog license shall be issued to any person unless he presents a certificate from a licensed veterinarian indicating that the dog has been immunized against rabies or hydrophobia within the preceding twelve months.

Maryland

Bills Introduced.—S. 5, to amend the law relating to narcotic drugs, proposes to include the drugs, isonipacaine, amidone and dromoran within the definition of "narcotic drugs" together with synthetic drugs having comparable habit-forming qualities. S. 19, to amend the law relating to rabies, proposes that when a dog subject to rabies has bitten any person it shall be the duty of any person having a knowledge of such fact to report the same to the county health officer who shall see that such dog is confined for such period of time as the health officer shall direct.

Massachusetts

Bill Introduced.—S. 482, proposes that after medical examiners and associate medical examiners have completed a seven year term they shall, if reappointed, hold their offices during good behavior. At the time of being reappointed they shall show aptitude for the work and be certified by an accredited medical college as having done graduate study in medico-legal investigation under qualified authority.

Michigan

Bills Introduced.—H. 286, proposes to authorize the board of supervisors of counties having a population of over 500,000 to abolish the office of coroner and create the office of county medical examiner. S. 240, proposes regulations for the licensing of trained certified graduate professional nurses, practical nurses, and trained attendants.

New Jersey

Bills Introduced.—A. 265, proposes to prohibit the sale of any drug or medicinal preparation or appliance intended to prevent the spread of venereal disease except by duly licensed practitioners of medicine or in pharmacies or drug stores, for whose operation a permit has been duly issued by the board of pharmacy. A. 288, to amend the workmen's compensation law, proposes among other things that an injured employee may, when care is required, select to treat him any duly licensed physician and proposes that if the employee is unable to do so, or elects not to do so, the employer shall promptly provide him with the necessary medical care.

Rhode Island

Bills Introduced.—H. 586, proposes to make it an obligation of the state to provide state paid hospital and medical services for all state employees. H. 605, proposes the creation of a special commission to make an intensive study of the state laws relating to narcotics. H. 636, proposes the creation of a special commission to make a complete study of the Rhode Island temporary disability insurance act.

Virginia

Bills Introduced.—S. 196, proposes to prohibit the sale of drugs, medicines and appliances for the prevention of venereal disease except by duly licensed practitioners of medicine or in pharmacies and retail stores which have obtained a permit from the state board of pharmacy. S. 227, to amend the medical practice act, proposes regulations authorizing the licensure of persons who graduate from foreign medical schools. S. 278, to amend the medical practice act, proposes to authorize persons who are interning or taking residency training within the state to extend the three-year period of training for two additional years before being required to obtain a license to practice medicine.

APPOINT FIELD DIRECTOR FOR COUNCIL ON RURAL HEALTH

Mr. Aubrey D. Gates has been appointed to the permanent staff of the Council on Rural Health to serve as Field Director, effective Feb. 1. The Council on Rural Health hopes that the state medical societies and the state committees on rural health will take full advantage of Mr. Gates' services whenever possible. His headquarter's address will be 1801 N. Polk St., Little Rock, Ark. In making the announcement, Dr. F. S. Crockett, Chairman of the Council, said "It is our intent to have Mr. Gates spend practically all of his time in the field. He will want to contact the headquarters offices of the state medical societies, the extension workers in the state land-grant agricultural colleges, leaders in agriculture and other organizations interested in the program of rural health."

MEDICAL NEWS

ALABAMA

Annual Stuart Graves Lecture.—Dr. Alton Ochsner, Henderson Professor of Surgery and head of the department of the Tulane University of Louisiana School of Medicine, New Orleans, will deliver the annual Stuart Graves Memorial Lecture of the Nu Sigma Nu medical fraternity at the Medical College of Alabama, Birmingham, on March 18.

Public Health Institute.—The Dental Service of the Veterans Administration Hospital at Tuskegee will present an Institute of Public Health in the auditorium of Tuskegee Institute March 16-19. Collaborating agencies include the state departments of public health, welfare, and vocational rehabilitation, the Tennessee Department of Public Health, various groups associated with Tuskegee Institute, the U. S. Public Health Service and Department of Agriculture, and the University of Alabama. About 40 speakers will participate in the program.

COLORADO

Personals.—Dr. Joseph E. Cannon, Providence, R. I., has been appointed chief of the tuberculosis section of the state health department.—Dr. John D. Gillaspie has been named mayor of Boulder by the city council, while Dr. James E. Donnelly was accorded a similar honor at Trinidad.

Health Broadcasts for School Children.—The Colorado State Medical Society's popular mystery-drama series, "Dr. Tim, Detective," is being released the week of Feb. 24. It will be carried by 13 stations and will be broadcast weekly for 13 weeks. Designed for school youngsters in the sixth, seventh, and eighth grades, "Dr. Tim" is also popular with other age groups and with parents. Again this year it has strong support from school officials, women's clubs, Parent Teachers Association groups, and from the medical profession and the woman's auxiliaries. "Dr. Tim" won a national award in 1950 at Ohio State University's Institute of Education Through Radio.

CALIFORNIA

Colver Research Foundation.—A dinner in honor of Dr. Benton Noble Colver, for many years head of the department of otolaryngology, College of Medical Evangelists, Loma Linda-Los Angeles, was given at the Biltmore Hotel in Los Angeles, Jan. 20. The heads of the teaching department of the college and a large number of otolaryngologists of Southern California were present. On this occasion the Colver Research Foundation was inaugurated. It was formed by subscriptions and gifts of former students, associates, and hosts of friends to stimulate research in otorhinolaryngology.

CONNECTICUT

Rickettsialpox.—Dr. James C. Hart, Connecticut Department of Health, has reported a localized outbreak of rickettsialpox, which occurred among occupants of an apartment house. These are the first cases to be reported in Connecticut. Large numbers of house mice, *Mus musculus*, and mites, *Allodermanyssus sanguineus* Hirst, were found in the apartment house.

Annual County Society Conference.—The Connecticut State Medical Society will sponsor its annual conference for county medical association officers March 20 in New Haven. The program will include talks and discussions on membership services, professional relations with hospitals, medical public relations, and the program of the American Medical Education Foundation.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

GEORGIA

Medical Assembly and Surgical Congress.—The Atlanta Grate Medical Assembly of the Fulton County Medical Society will be held in the New Auditorium of the Biltmore Hotel, Atlanta, March 10-13. The Southeastern Surgical Congress meet in the Georgian Ball Room at the Biltmore on the same dates. Out-of-state speakers and their subjects for the general assembly include:

Edward H. Ryneerson, Rochester, Minn., Is Obesity an End Problem?

George E. Shambaugh Jr., Chicago, Management of Deafness.
Hugh McCulloch, Chicago, Rheumatic Fever and Rheumatic Disease.

George E. Burch, New Orleans, Diseases of the Heart. Diseases of the Kidney.

Edward G. Waters, Jersey City, Arterial Ligation for Post Partum Hemorrhage.

John L. Emmett, Rochester, Minn., Therapy in Genitourinary Infection.

Nicholson J. Eastman, Baltimore, subject to be announced.

Shields Warren, Boston, Acute Radiation Syndrome.

Cornelius P. Rhoads, New York, Clinical Endocrinology and the Problem of Diabetes.

Francis D. Moore, Boston, Metabolic Response to Surgery and the Modern Treatment of Burns.

Joe V. Meigs, Boston, subject to be announced.

Albert M. Snell, Palo Alto, Calif., subject to be announced.

There will be a symposium on diseases of the liver on Monday, a symposium on cardiac and hypertensive states on Tuesday and another on gastroenterology on Wednesday.

Out-of-section speakers of the surgical congress include:

John deJ. Pemberton, Rochester, Minn., Carcinoma of the Thyroid.

Claude S. Beck, Cleveland, Operation for Coronary Occlusion.

George Crile Jr., Cleveland, Surgical Treatment of Ulcerative Disease of the Colon.

One registration fee of \$15 will admit a physician to all assemblies.

INDIANA

Medical-Civic Dinner.—The Vanderburgh County Medical Society will hold its first annual medical-civic dinner March 15 in the Rose Room of the Hotel McCurdy in Evansville. Certificates of appreciation will be awarded to all living past presidents of the society. About 100 leading business and civic leaders will be guests. Frank Sparks, president of Wabash College, Muncie, will be the principal speaker.

KANSAS

Annual Porter Lectures.—Dr. Otto Loewi, research professor of pharmacy, New York University College of Medicine, will deliver the 19th annual Porter Lectures at the Kansas University Medical Center and on the Lawrence campus. At 4 p. m. on March 31 at the university, he will speak "Problems in the Field of Adrenal Function." On April 11 a. m. in Strong Hall on the Lawrence campus, his subject will be "From the Workshop of Discoveries." He will speak "Mechanism of Drug Action" at the medical center April 12 at 4 p. m. In addition, Dr. Loewi will address the medical students in Kansas City Monday noon March 31 on "Reflections on the Study of Medicine." Funds for the Porter Lectures were provided by a bequest of the late Dr. J. L. Porter of Paola, Kan.

KENTUCKY

Retiring Physician Honored.—Dr. Alice N. Pickett, head of the obstetrics department of the University of Louisville School of Medicine for 25 years and professor emerita for 5 years, will be honored by a testimonial dinner at the Brown Hotel, Louisville, Jan. 28, by the Louisville Obstetrical and Gynecological Society. A silver dish was presented her by the society on her retirement as an obstetrician.

Personal.—Dr. Joseph A. Little, Louisville pediatrician, has been named to serve as medical director of the Kentucky Children's Commission on a part time basis by contract between the commission and the University of Louisville School of Medicine.

of Medicine. He will supervise the medical programs of the commission at Kosair Crippled Children Hospital in Louisville, and Cardinal Hill Convalescent Hospital in Lexington, as well as programs in Covington, Ashland, Owensboro, and Paducah.

LOUISIANA

Psychosomatic Problems in Children.—The first meeting of the Psychosomatic Forum of New Orleans will be held at 8:30 a. m. Feb. 28 in the board room of the Orleans Parish Medical Society, New Orleans. Papers on psychosomatic problems in children will be given by Drs. Irwin M. Marcus, Ian Stevenson, and Clifford G. Grulee Jr., all of New Orleans. The subjects covered will include enuresis, diabetes, and infantile colic. Drs. Ralph V. Platou and Myron E. Wegman, New Orleans, will participate with the speakers in a panel discussion following presentation of the papers.

MARYLAND

New State Medical Journal.—The *Maryland State Medical Journal* began publication with the January issue. It will report the activities of the Medical and Chirurgical Faculty of the State of Maryland, its publisher, incorporating the faculty's former *Bulletin* and *Newsletter*. The editor is Dr. George H. Yeager, Baltimore. The faculty has had other official publications. From October, 1839, to June, 1843, it published the *Maryland Medical and Surgical Journal* and *Official Organ of the Medical Department of the Army and Navy of the United States*. From May, 1887, to March, 1918, a publication known as the *Maryland Medical Journal* carried the notes and communications of the faculty. For a brief period, 1905-1908, it became the official publication medium of the faculty and included transactions. In 1908 the house of delegates terminated its contract with the *Maryland Medical Journal* and initiated an official monthly *Bulletin*, which was discontinued in 1922. The new journal is similar in format to other state medical journals issued by state medical associations. It is a member of the State Journal Advertising Bureau.

MASSACHUSETTS

Personal.—Dr. William C. Moloney, clinical professor of medicine, Tufts College Medical School, and assistant director of the first and third (Tufts) Medical Services at the Boston City Hospital, will leave Boston with his family for Hiroshima, Japan, April 1. He will serve for the next two years as internist with field units of the Atomic Bomb Casualty Commission, which are engaged in the study of the effects of atomic radiation in Hiroshima and Nagasaki. This work is under the direction of the National Research Council and the National Academy of Science.

Bay State Rehabilitation Conference.—The second annual Bay State Rehabilitation Conference will be held March 12 at the Copley Plaza Hotel, Boston. The morning discussion will center around manpower and rehabilitation and what can be done to encourage employment of the handicapped. Harry E. Howard, personnel manager at the Norton Company, Worcester, will be chairman. The afternoon subject will be "Helping Them to Help Themselves." A clinical demonstration will be introduced by Dr. Joseph S. Barr, chief of orthopedic service at Massachusetts General Hospital. Cases will be presented and discussed by Drs. Henry H. Kessler, West Orange, N. J.; Elmer F. Franseen, Springfield; Robert C. Hartson, Worcester; William E. Kenney, Fall River, and Arthur L. Watkins, Boston.

MICHIGAN

Ford Hospital Appointments.—Dr. Lawrence S. Fallis has been appointed surgeon-in-chief and Dr. John G. Mateer, physician-in-chief at Henry Ford Hospital, Detroit. Dr. Fallis, who succeeds the late Dr. Roy D. McClure, has been on the staff of the hospital since 1925. Dr. Mateer succeeds Dr. Frank J. Sladen, who retired Feb. 1 as head of the department of medicine, a post he had held since the hospital was organized by the late Henry Ford in 1915. Dr. Mateer joined the staff of the hospital in charge of the division of gastroenterology in 1920.

NEW YORK

Roswell Park Medal.—On Feb. 14 the Buffalo Surgical Society presented the fifth Roswell Park Memorial Medal for "outstanding surgical achievement" to Dr. Edward D. Churchill of Boston. He delivered the annual Roswell Park Lecture entitled "The Architectural Basis of Pulmonary Ventilation."

Postgraduate Instruction.—Three postgraduate lectures have been arranged for the Rensselaer County Medical Society to be given in Troy Tuesday evenings at 8:30 p. m. as follows:

March 11, Samaritan Hospital, Leon G. Berman, Syracuse, Diagnosis and Treatment of the Acute Surgical Abdomen.

April 8, Leonard Hospital, Marvin Stern, Brooklyn, Recognition and Management of Psychiatric Problems in General Practice.

May 6, St. Mary's Hospital, Emil Granet, New York, Recent Progress in the Management of Common Anorectal Lesions.

This instruction has been arranged by the Medical Society of the State of New York in cooperation with the New York State Department of Health.

New York City

Annual Elsberg Lecture.—Dr. Gilbert Horrax, Boston, will deliver the annual Charles A. Elsberg Lecture of the New York Society of Neurosurgery March 18 at 8:30 p. m. in the New York Academy of Medicine Building. His subject will be "The Development of Brain Tumor Surgery." Dr. Horrax is neurosurgeon to the New England Deaconess and New England Baptist hospitals, Boston.

Mount Sinai Hospital Centennial.—Mount Sinai Hospital on Jan. 16 opened the year long observance of its 100th anniversary. The year will be marked by an historical exhibit, a symposium on medicine and society, publication of the history of the hospital, and dedication of the hospital's first maternity pavilion and two new laboratory buildings. The hospital had its first home in a four-story building with a 45 bed capacity. It was incorporated on Jan. 16, 1852, as the first Jewish sponsored hospital in the United States, and opened its doors to the first patient in May, 1855. In its first year the hospital treated 225 patients at a cost of \$5,493. Today it treats 40,000 a year and its annual operating cost is \$5,500,000.

NORTH CAROLINA

Narcotic Violations.—Dr. Marvin A. Bowers, Winston-Salem, pleaded *nolo contendere* in the United States District Court at Winston-Salem, and has been placed on probation for a period of five years and fined \$1,000.—Dr. Robert H. Freeman, Raleigh, pleaded guilty to a violation of the federal narcotic law and on Dec. 13, 1951, was sentenced to a term of three years.

OHIO

Personal.—Dr. Elmore R. McNeal, Youngstown, has been appointed editor of the *Mahoning County Medical Society Bulletin*, succeeding Dr. Stephen W. Ondash, Youngstown, who will continue to serve as one of the associate editors.

Academy Members Awarded Fifty-Year Pins.—The Cincinnati Academy of Medicine in December honored 13 members. The 9 physicians who were presented 50 year membership pins are Drs. Martin H. Fischer, Tilden J. Beck, George S. Buttemiller, Thomas Hulick, William E. Leever, Francis M. Oxley, Frederick C. Theiss, Harry J. Wittenberg, and Henry L. Woodward. Pins were presented to members of the families of Drs. John P. Beneke, William L. Brodberger, George A. Pierret, and Joseph S. Podesta. At the scientific session Dr. Alan R. Moritz, professor of pathology at Western Reserve University, Cleveland, spoke on problems of crime detection.

OKLAHOMA

General Practitioners Meeting.—The second annual meeting of the Oklahoma Academy of General Practice will be held at the Tulsa Hotel March 16-18. The scientific program beginning on Monday includes a seminar on juvenile delinquency Stanley R. Truman, Oakland, Calif., as moderator. Edward D. Greenwood, Topeka, Kan., Dr. Miss Elba L. Dyer, and Mr. Howard M.

Mr. Buck Cook, Oklahoma City, as speakers. Guest speakers at the convention include Drs. Vincent J. Derbes, New Orleans; John F. Holt, Ann Arbor, Mich.; Louis J. Regan, Los Angeles; Drs. Truman and Greenwood; F. A. Duncan Alexander, McKinney, Texas, and William Gordon, Lubbock, Texas, Dr. Truman will also speak at the dinner meeting Monday at 7 p. m.

PENNSYLVANIA

Personal.—Dr. Louis G. Fetterman, Hershey, has been appointed medical director of the York Corporation at the company's new medical center. He has been industrial physician in the medical department of Hershey Estates in Hershey.

Study on Child Health.—A \$55,000 study designed to stimulate correction of health defects in school children will be conducted by Pennsylvania State College, with a \$35,000 grant from the Health Information Foundation, New York. The research project, to be conducted in selected schools in 22 representative communities of Pennsylvania, is scheduled for completion in Aug., 1953. It will develop and test techniques to influence school children and parents "to have treatment for pathological conditions discovered by school health examinations."

Philadelphia

Personal.—At a recent meeting of the Pennsylvania Public Health Association Dr. Pascal F. Lucchesi, professor and head of the department of public health, Hahnemann Medical College and Hospital of Philadelphia, was awarded a certificate for meritorious service in the field of public health in Pennsylvania during the year 1951.

Joint Meeting of Pathology.—The section on clinical pathology of the Philadelphia County Medical Society and the Pathological Society of Philadelphia will hold their annual joint meeting at the Philadelphia County Medical Society building March 13. Out-of-state speakers and their subjects include Drs. Richard Ford of Boston, "The Relationship of Trauma and Subarachnoid Hemorrhage," and Emil Novak of Baltimore, "Hydatidiform Mole and Chorionepithelioma." The guest speaker at the banquet in the Union League of Philadelphia at 6 p. m. will be Hugh D. Cott, Jr. of Philadelphia, member of the House of Representatives of the U. S. Congress.

Pittsburgh

Gift to Aid Psychiatric Research.—The A. W. Mellon Educational and Charitable Trust has given \$250,000 to the University of Pittsburgh to aid the five-year program of the Western Psychiatric Institute and Clinic. Additional funds for the program have been received from the Maurice and Laura Falk Foundation (\$250,000), the Sarah Mellon Scaife Foundation (\$75,000), and the Howard Heinz Endowment (\$25,000). Three specialists are participating in the research of the institute: Henry W. Brosin, medical director; I. Arthur Mirsky, head of the research division; and Benjamin Spock, professor of child development.

TENNESSEE

Personal.—Dr. Jack N. Hunt, senior lecturer in physiology at Guy's Hospital Medical School, London, England, has been sent to the University of Tennessee College of Medicine, Memphis, for a protracted period by the Rockefeller Foundation. Dr. Hunt, who has made studies on the function of the digestive tract, will continue to make investigations in this field working with the research group of Dr. Joseph P. Quigley, chief of the division of physiology.

Increase Tuition Fees.—An increase in fees effective July 1 for students in medicine, dentistry, and pharmacy at the University of Tennessee Medical Units in Memphis has been announced by the university president. The increase of \$25 per quarter for medical and dental in-state students and \$18.50 for pharmacy in-state students was made to meet steadily rising costs of instruction. It is the first increase in these fees since 1942. The new quarterly fee schedule is as follows: medicine, in-state \$150, out-of-state \$225; dentistry, in-state \$125, out-of-state \$175; pharmacy, in-state \$97.50, out-of-state \$125.

WEST VIRGINIA

Surgeons' Meeting.—The West Virginia Chapter of the American College of Surgeons will sponsor a two-day meeting at the Greenbrier in White Sulphur Springs March 28-29. Doctors serving a residency in West Virginia hospitals will be invited to submit papers. An award of \$100 will be given for the best paper, \$75 for the second best, and \$75 for the third. The papers will be read at the meeting and the awards made at that time. Dr. William R. Laird of Montgomery is West Virginia governor of the college.

WISCONSIN

Dedicate New Cancer Wing.—The new cancer patient wing of the State of Wisconsin General Hospital was dedicated Jan. 23 at the University of Wisconsin, Madison. Financed by a grant of \$975,000 from the federal government, the new wing will house outpatient service (chemosurgery and dermatology), chemical and pathological laboratories, the university hospital's tumor clinic, and rooms for patients. The wing connects with McArdle Memorial Laboratory for Cancer Research and is adjacent to the new million-volt x-ray machine for treating cancer patients. Chief speaker was Dr. Leonard Scheele, surgeon general of the U. S. Public Health Service.

County Health Council Movement.—The state medical society reports that the county health council movement is growing rapidly in the state. The councils have no official status, but they represent a potent force in local influence. The Barron County Public Health Council, which is working on the eradication of brucellosis, is about to become a health division of the Barron County Community Council. Some of the other county council and their programs are as follows:

Outagamie County, a health improvement program built around eight major health needs discovered in the 1950 health census; county-wide immunization education project.

Dane County, continuation of the diabetic survey into 1952.

Brown County, selection of a health commissioner for the city of Green Bay.

Polk County, fluoridation of their public water supply, three cities now having plans to install the equipment; preschool health program; procurement of a second public health nurse for the county, the county paying for the first year's salary and agreeing to pay all her expense.

Ozaukee County, mental health education program.

Health councils have the endorsement and active support of the state medical society. Most local councils count physicians among their membership to serve in an advisory capacity. Other health personnel are also prominent in many councils.

GENERAL

International Congress on Diabetes.—Persons interested in the First International Congress of the International Diabetes Federation to be held at Leyden, Netherlands, July 7-12 are requested to apply for a prospectus to Dr. Elliott P. Joslin, honorary president of the American Diabetes Association, Bay State Road, Boston 15. Completed application forms should be received by the executive secretary at the Hague on or before April 1, 1952.

WHO Seeks Personnel for Foreign Medical Schools.—In a program of promoting improved medical education throughout the world, the World Health Organization has been asked several countries (among them Pakistan, India, the Philippines, Iran, and Singapore) to obtain professors for two or more years in anatomy, physiology, pharmacology, and pathology. There also is a position open as principal of a medical college in India for which persons with experience in the administration of medical schools are eligible. Persons interested in any of the positions may write directly to the World Health Organization, Geneva, Switzerland, for details.

Aero Medical Association Meeting.—This association will hold its annual international meeting at the Statler Hotel March 17-19 in Washington, D. C., under the presidency of Maj. Gen. Har G. Armstrong, USAF Surgeon General. Scheduled to attend and participate in the meeting for the first time are leading aviation medicine representatives from 20 nations, including Yugoslavia, Italy, Belgium, Denmark, Norway, and Sweden. A program of scientific papers, exhibits, and demonstrations will delineate

many of the latest trends and developments in the field of aviation medicine. The space medicine group of the association has scheduled a series of discussions in their specialized field of research.

Paraplegia Foundation Fellowships.—The National Paraplegia Foundation announces the continuation of a limited number of fellowships for research in spinal cord disease and trauma and in the complications commonly associated with such disease or injury. These fellowships carry a minimum stipend of \$3,000 per year and may be awarded to any candidate who has demonstrated a capacity for medical research and has outlined a program of meritorious study. The fellowships will be awarded by the medical advisory committee and are open for the academic year 1952-1953. Applications, which may be obtained from the chairman of the medical advisory committee, should be submitted not later than May 1.

Multiple Sclerosis Society Fund Drive.—A drive to raise \$425,000 for research and service programs concerning multiple sclerosis was launched Feb. 8 by the National Multiple Sclerosis Society, 270 Park Ave., New York. Over half of the money raised will be spent to continue and expand research in multiple sclerosis and related nerve diseases. The remainder will be spent to further the society's educational and service program among physicians, patients, and the public. An estimated 250,000 persons in the United States have the disease. Seventeen research projects, including seven treatment and research clinics in leading medical centers of the country, have been supported by the society at a total cost of \$444,000.

National Health Council Meeting.—At the annual meeting of the National Health Council in the Hotel Roosevelt, New York, March 13-14 the subject under discussion will be "What's in the Health Council Idea?" The program has been arranged around three health symposiums as follows:

Citizen Participation in Community Health Planning Through Community Health Councils, Margaret A. Hickey, LL.B., St. Louis, moderator.

Health Planning for the Future, Albert W. Dent, LL.D., New Orleans, moderator.

Health Planning and Action on the State Level Through State Health Councils, Robin C. Buerki, Philadelphia, moderator.

At the annual luncheon at 12:30 p. m. the Honorable Williard L. Thorp, assistant secretary of state for economic affairs of the U. S. State Department, will speak on "Health and Geography."

Kenfield Memorial Award.—Competition for the 1952 Kenfield Memorial Scholarship will open March 1, according to the American Hearing Society, administrator of the annual award to a prospective teacher of lipreading to the hard of hearing. Applications are to be mailed by May 1 to Miss Rose Feilbach, chairman of the Society's Teachers' Committee, 1157 N. Columbus St., Arlington, Va. A winner of the award is entitled to take a teacher's training course in lip reading from any normal training teacher, school, or university in the United States offering a course acceptable to the society's teachers' committee. Specifications for a hard of hearing applicant include 30 clock hours of private instruction under an approved teacher of lipreading or 60 clock hours of instruction in public school classes under an approved teacher of lipreading.

Incidence of Measles Still Increasing.—The incidence of measles increased during the week ended Feb. 2 as compared with the previous week. The cumulative total for the first five weeks of 1952 is now 76,728 as compared with 43,034 for the same period of 1951. Since 1935 the cumulative total for the first 5 weeks exceeded that for 1952 only in 1938, when there were 98,936 reported cases. In 1944 the cumulative total for the same period was 68,499 and in 1949 it was 69,293. The incidence during the current period has been concentrated in the northeastern part of the country, 65% of the cases being reported by the New England and Middle Atlantic states. In 1949 the disease was more widespread, and, although large numbers were reported in these same states, they constituted only 34% of the total reported during the first five weeks of the year. In 1949 the peak in reported cases was reached in the week ended March 26, and in 1951 the peak was reached in the week ended May 2.

Inter-American Cardiological Congress.—The fourth Inter-American Cardiological Congress will be held in Buenos Aires from August 31 to September 7, under the auspices of the Argentine government. Those who wish to participate in it as titular members must ask for their registration before April 1 and pay a fee of 250 pesos. Their relatives who wish to be registered as associate members will pay a fee of 100 pesos. Members who wish to give papers must submit before April 1 a summary of each work that must not exceed 200 words, and if possible, should be written in Spanish or Portuguese and in English. Summaries should be sent by way of the national society of cardiology to which the member belongs (or directly if there is no society of cardiology in his country). All correspondence should be addressed to the Administrative Secretary's Office of the Congress, Larrea 1132, Buenos Aires.

Conference on Prevention of Blindness.—Some 500 prevention of blindness workers from all parts of the United States, Canada, and other countries will meet at the Mellon Institute in Pittsburgh March 19-21 for the 43rd conference of the National Society for the Prevention of Blindness. Dr. Edmond R. McCluskey, professor of pediatrics, University of Pittsburgh School of Medicine, will be chairman Wednesday morning of the discussion on children's eye problems, which will include such topics as correction of muscle imbalance, detecting and correcting visual defects among preschool children, and environmental factors in visual efficiency. On Wednesday afternoon, under the chairmanship of Dr. Conrad Berens of New York, reports will be heard on the present status of corticotropin (ACTH) and cortisone, survey of vision loss in New York state due to retrolental fibroplasia, management of congenital glaucoma, hereditary eye conditions, and relationship of clinical research and fundamental research. Thursday morning the conference will be concerned with sight conservation in industry. The chairman will be Dr. J. Huber Wagner of the United States Steel Corporation, Pittsburgh. In the afternoon on Thursday there will be separate group discussions for teachers, nurses, and social workers. A dinner is scheduled for Thursday evening. Friday morning's program will deal with eye problems of middle age.

Academy of General Practice Meeting.—The fourth annual scientific assembly of the American Academy of General Practice will be held in Atlantic City, N. J., March 24-27 under the presidency of Dr. Jason P. Sanders, Shreveport, La. The program will center around symposiums dealing with specific medical problems. More than 30 teachers will take part. Public relations as it concerns the family doctor will be discussed at the opening of the scientific program on Monday afternoon. Speakers will include Dr. John W. Cline, San Francisco, President of the American Medical Association; Leonard E. Read of Irvington, N. Y.; Louis B. Seltzer of Cleveland, and Rollen Waterson of Oakland, Calif. A roundtable discussion "You and Your Public" will follow, with Dr. John S. DeTar of Milan, Mich., serving as moderator. A paper on medical problems of teen-agers will be given by Dr. O. Spurgeon English, Temple University, Philadelphia, and another on the problems of persons between 40 and 50 years old will be given by Dr. Richard A. Kern, also of Temple University. Tuesday morning's program will deal with the problem drinker. Seldon D. Bacon, Ph.D., of Yale University, New Haven, Conn., will begin with a short analysis of "Who and Why," and Dr. Harold W. Lovell, New York, will take up medical treatment designed to hasten return to physiologic normalcy. A co-founder of Alcoholics Anonymous will round out the formal lecture with a discussion of rehabilitation. This will be followed by a panel discussion on problem drinking with Dr. Andrew S. Tomb Jr. of Victoria, Texas, serving as moderator. The Tuesday afternoon program will deal with medical advancement in obstetrics. Dr. Walter Dameshek of Boston will speak on "Treatment and Mistreatment of Anemia." Wednesday morning's program will deal with advancements in medicine. Research trends will be discussed by Dr. Cyril M. MacBryde of St. Louis. Dr. Hans Selye, director of the Institute of Experimental Medicine and Surgery at the University of Montreal, will speak on "Stress Reactions in Health Disease." He will be followed by Dr. Jerome W. Conn of the University of Michigan Medical School, Ann Arbor, who will speak on "Practical Applications in General Medicine."

answer period will close the afternoon program with Dr. Harry Gold of New York serving as moderator. Lectures on orthopedics and orthopedic problems will be given Thursday. The banquet speaker Wednesday evening will be Kenneth McFarland of Topeka, Kan., educational director for American Trucking Associations, Inc., and educational consultant for General Motors. Scientific exhibits will be keyed to each lecture subject. Many of the 179 firms in the technical exhibit will also relate their exhibits to the scientific program.

FOREIGN

British Congress of Obstetrics and Gynecology.—This congress will be held July 8-11 at the University of Leeds, England, under the presidency of Prof. Andrew Claye. The first paper will be by the guest speaker Prof. M. A. Bastiaanse of Holland, on "Cancer of the Body of the Uterus." Other papers to be presented include:

Abnormal Uterine Action During Labor, G. H. Bell, Dundee, W. C. W. Nixon, London.

Place of the Pediatrician in a Maternity Unit, W. Gaisford, Manchester, Mr. F. Stabler, Newcastle.

Stress Incontinence of Urine, A. H. Aldridge, New York, T. N. A. Jeffcoat, Liverpool.

Genital Tuberculosis in the Female, Magnus Haines, London, Mr. John Stallworthy, Oxford.

Membership forms may be secured through one of the secretaries, Brian Jeaffreson, The Hospital for Women, Coventry Place, Leeds.

DEATHS IN OTHER COUNTRIES

Professor Henri Hartmann, Paris, for 32 years professor in the French Faculty of Medicine, died January 3, aged 91, of a heart attack, according to the *New York Times*. He was one of the two founders in 1918, and a former president of the French League Against Cancer, and a former president of the French Academy of Medicine. He was president of the Association for the Development of Medical Relations between France and other countries and a Grand Officer of the Legion of Honor. During World War I he performed many operations on wounded soldiers in Paris hospitals.—**Frederick Murgatroyd**, Ch.B., who was appointed a little over a year ago to the Wellcome Chair of Clinical Tropical Medicine at the University of London, died December 16. Dr. Murgatroyd had been on the faculty of the Liverpool School of Tropical Medicine from 1927-1937, when he joined the School of Hygiene and Tropical Medicine in London as a lecturer.

MEETINGS

AERO MEDICAL ASSOCIATION, Washington, D. C., March 17-19. Dr. Thomas H. Sutherland, 214 South State St., Marion, Ohio, Secretary.

ALABAMA MEDICAL ASSOCIATION OF THE STATE OF, Montgomery, April 17-19. Dr. Douglas L. Cannon, 519 Dexter Ave., Montgomery, Secretary.

AMERICAN ACADEMY OF FORENSIC SCIENCES, Biltmore Hotel, Atlanta, Ga., March 6-8. Prof. Ralph F. Turner, Michigan State College Dept. of Police Administration, East Lansing, Mich., Secretary.

AMERICAN ACADEMY OF GENERAL PRACTICE, Atlantic City, N. J., March 24-27. Mr. Mac F. Cahal, 406 West 34th St., Kansas City 2, Mo., Executive Secretary.

AMERICAN ASSOCIATION OF ANATOMISTS, Providence, R. I., March 19-21. Dr. Normand L. Hoerr, 2109 Adelbert Road, Cleveland 6, Secretary.

AMERICAN ASSOCIATION OF PATHOLOGISTS AND BACTERIOLOGISTS, New York, April 10-12. Dr. Alan R. Moritz, 2085 Adelbert Road, Cleveland 6, Secretary.

AMERICAN ASSOCIATION OF RAILWAY SURGEONS, Drake Hotel, Chicago, April 1-3. Dr. Chester C. Guy, 5800 Stony Island Ave., Chicago 37, Secretary.

AMERICAN COLLEGE OF ALLERGISTS, William Penn Hotel, Pittsburgh, April 7-9. Dr. Fred W. Wittich, 423 LaSalle Medical Bldg., Minneapolis 2, Secretary.

AMERICAN COLLEGE OF SURGEONS, SECTIONAL MEETINGS: Minneapolis, Radisson Hotel, March 24-26. Dr. Harvey Nelson, 78 South 9th St., Minneapolis 2, Chairman.

Tucson, Ariz., Pioneer Hotel, April 7-9. Dr. Meade Clyne, 110 South Scott St., Tucson, Chairman.

Vancouver, B. C., Vancouver Hotel, March 31-April 4. Dr. J. Russell Neilson, 925 West Georgia St., Vancouver, B. C., Chairman.

AMERICAN CONGRESS ON OBSTETRICS AND GYNECOLOGY, Netherlands-Pt Hotel, Cincinnati, March 31-April 4. Dr. Luella E. Nadelhoffer, South Michigan Ave., Chicago 3, Secretary.

AMERICAN HEART ASSOCIATION, Hotel Statler, Cleveland, April 17-20. William H. Bunn, 1775 Broadway, New York 19, Secretary.

AMERICAN ORTHOPSYCHIATRIC ASSOCIATION, Chalfonte-Haddon Hall, Atlantic City, N. J., Feb. 25-27. Dr. Nina Ridenour, 25 West 54th New York 19, Secretary.

AMERICAN PSYCHOSOMATIC SOCIETY, Chicago, March 29-30. Dr. Frederic C. Redlich, 551 Madison Avenue, New York 22, Secretary.

AMERICAN SOCIETY FOR EXPERIMENTAL PATHOLOGY, New York, April 14. Dr. Russell L. Holman, 1542 Tulane Ave., New Orleans 12, Secretary.

AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, New York, April 14-18. Elmer H. Stotz, 260 Crittenden Blvd., Rochester, N. Y., Secretary.

AMERICAN SURGICAL ASSOCIATION, White Sulphur Springs, W. Va., 16-18. Dr. Nathan A. Womack, University Hospitals, Iowa City, Secretary.

CENTRAL SURGICAL ASSOCIATION, Toronto, Can., March 6-8. Dr. James Priestley, 102 Second Avenue S.W., Rochester, Minn., Secretary.

CHICAGO MEDICAL SOCIETY ANNUAL CLINICAL CONFERENCE, Palmer Hotel, Chicago, March 4-7. Dr. Walter C. Bornemeier, 86 East Randolph Chicago 1, Secretary.

JOHN A. ANDREW CLINICAL SOCIETY, Memorial Hospital, Tuskegee Institute, Ala., April 6-12. Dr. Eugene H. Dibble Jr., Memorial Hospital, Tuskegee Institute, Secretary.

MICHIGAN CLINICAL INSTITUTE, Book-Cadillac Hotel, Detroit, March 1. Dr. E. F. Sladek, 123 E. Front St., Traverse City, Chairman.

MISSOURI STATE MEDICAL ASSOCIATION, Hotel Jefferson, St. Louis, Mo., 30-April 2. Dr. H. E. Petersen, 634 North Grand Blvd., St. Louis, Secretary.

NATIONAL CONFERENCE ON RURAL HEALTH, Shirley-Savoy Hotel, Detroit, Feb. 28-Mar. 1. Dr. F. S. Crockett, 535 North Dearborn St., Chicago, Chairman.

NEW ORLEANS GRADUATE MEDICAL ASSEMBLY, Municipal Auditorium, Orleans, March 10-13. Dr. Woodward D. Beacham, 1430 Tulane Room 105, New Orleans 12, Secretary.

NORTH PACIFIC SOCIETY OF INTERNAL MEDICINE, Portland, Ore., March 1. Dr. R. L. King, 1115 Terry Ave., Seattle 1, Secretary.

PACIFIC COAST SURGICAL ASSOCIATION, Del Monte, Calif., Feb. 26-29. Carleton Mathewson Jr., Stanford University Hospital, San Francisco, Secretary.

PIEDMONT PROCTOLOGIC SOCIETY, Charlotte, N. C., March 29-30. I. Richard Jackson, 224 Hillsboro St., Raleigh, N. C., Secretary.

POST GRADUATE INSTITUTE OF THE PHILADELPHIA COUNTY MEDICAL SOCIETY, Bellevue-Stratford Hotel, Philadelphia, April 1-4. Dr. Thomas Durant, 301 South 21st St., Philadelphia 3, Director.

SOUTHEASTERN ALLERGY ASSOCIATION, Bon Air Hotel, Augusta, Ga., 11-22. Dr. Katharine B. MacInnis, 1515 Bull St., Columbia 49, Secretary.

SOUTHEASTERN SECTION, AMERICAN UROLOGICAL ASSOCIATION, Boca Raton, Fla., April 2-5. Dr. Russell B. Carson, Sweet Bldg., Fort Lauderdale, Fla., Secretary.

SOUTHEASTERN SURGICAL CONGRESS, Atlanta, Ga., March 10-13. Benjamin J. Beasley, 701 Hurt Bldg., Atlanta 3, Ga., Secretary.

SOUTHWEST ALLERGY FORUM, Hotel Baker, Dallas, Texas, March 2-3. James Holman, Medical Arts Bldg., Dallas, Secretary.

TENNESSEE STATE MEDICAL ASSOCIATION, Andrew Johnson Hotel, Nashville, April 7-9. Mr. V. O. Foster, 504 Doctors Bldg., Nashville, Executive Secretary.

UNITED STATES-MEXICO BORDER PUBLIC HEALTH ASSOCIATION, Mon Nuevo Leon, Mexico, March 17-19. Dr. J. C. Ellington, 314 U. S. House, El Paso, Texas, Secretary.

WESTERN SOCIETY OF ELECTRO-ENCEPHALOGRAPHY, Del Monte Lodge, Beverly Hills, Calif., March 2-3. Dr. Nicholas A. Bercel, 450 North B Drive, Beverly Hills, Calif., Secretary.

INTERNATIONAL

AUSTRALASIAN MEDICAL CONGRESS, Melbourne Victoria, Australia, 22-30. Dr. C. H. Dickson, Medical Society Hall, 426 Albert St. Melbourne, Victoria, Australia, Hon. General Secretary.

COMMONWEALTH AND EMPIRE HEALTH AND TUBERCULOSIS CONFERENCE, Central Hall, London, England, July 8-13. Dr. J. H. Harley White, Tavistock House North, Tavistock Sq., London, W.C.1, England, Secretary-General.

CONGRESS OF THE INTERNATIONAL DIABETES FEDERATION, Leyden, Holland, July 7-12. Dr. F. Gerritzen, 33. Prinsegracht, The Hague, Holland, Secretary.

EUROPEAN CONGRESS OF CARDIOLOGY, University of London, Bloomsbury, W.C.1, England, Sept. 10-12. Dr. K. Shirley Smith, 35 Wimpole London, W.1, England, Secretary.

EUROPEAN SOCIETY OF CARDIOVASCULAR SURGERY, Strasbourg, France, 3-4. Sir James Learmonth, Department of Surgery, University Buildings, Edinburgh 8, Scotland.

INTER-AMERICAN CARDIOLOGICAL CONGRESS, Buenos Aires, Argentina, 31-Sept. 7. Dr. Blas Moia, Larrea 1132, Buenos Aires, Argentina, Secretary-General.

INTER-AMERICAN CONGRESS OF PUBLIC HEALTH, Havana, Cuba, Sept. 1. Pan-American Sanitary Bureau, 2001 Connecticut Ave., Washington, D. C.

INTER-AMERICAN CONGRESS OF RADIOLOGY, Mexico City, Mexico, Nov. 1. Dr. Guido Torres Martinez, Marsella No. 11, Mexico, D.F., Secretary-General.

INTERNATIONAL COLLEGE OF SURGEONS, Madrid, Spain, May 20-22. Max Thorek, 850 West Irving Park Road, Chicago, Ill., U. S., Secretary-General.

INTERNATIONAL CONGRESS OF COMPARATIVE PATHOLOGY, Madrid, May 4-11. Prof. Carda-Aparici, Calle Fernando VI.8, Madrid, Secretary.

INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY, London, England, July 21-26. Dr. Gordon B. Mitchell-Heggs, 5, Lisle St., London, W.C.2, England, General Secretary.

INTERNATIONAL CONGRESS ON DIABETES, Leyden, The Netherlands, July 7-12. Dr. F. Gerritzen, 33, Prinsegracht, The Hague, Netherlands.

INTERNATIONAL CONGRESS OF HAEMATOLOGY, Mar del Plata, Argentina, Sept. 21-26. Dr. Carlos Reussi, Anchorena 1710, Buenos Aires, Argentina, Secretary.

INTERNATIONAL CONGRESS OF HEALTH TECHNICIANS, Palais de la Mutualite, Paris, France, June 9-14. Secretariat General, 6 Square Desaix, Paris XV^e, France.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Friends House, London, N.W.1, Eng. Sept. 15-18. Sir Harold Boldero, 12 Pall Mall East, London, S.W.1, England, Secretary.

INTERNATIONAL CONGRESS OF LEGAL AND SOCIAL MEDICINE, Berne, Switzerland, April 15-18. Prof. J. Dettling, 20, Buhlstrasse, Berne, Switzerland.

INTERNATIONAL CONGRESS ON MEDICAL RECORDS, London, England, Sept. 7-12. Miss Gwen Perkins, 120 C Street S.E., Washington, D. C., Chairman.

INTERNATIONAL CONGRESS ON NEUROPATHOLOGY, Rome, Italy, Sept. 8-13. Dr. Armando Ferraro, 722 W. 168th St., New York, N. Y., U. S. A., Secretary General.

INTERNATIONAL CONGRESS OF OTO-NEURO-OPHTHALMOLOGY, Lisbon and Estoril, Portugal, April 22-26. Prof. Diogo Furtado, Servico de Neurologia, Hospital dos Capuchos, Lisbon, Portugal, General Secretary.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE, London, England, July 14-19. Dr. A. C. Boyle, 45, Lincoln's Inn Fields, London, W.C.2, England, Hon. Secretary.

INTERNATIONAL CONGRESS FOR THERMALISM AND CLIMATOTHALASSOTHERAPY, Nice-Cannes, France, April 3-8.

INTERNATIONAL SOCIETY OF GEOGRAPHIC PATHOLOGY, Liège, Belgium, July 15-18. Dr. Fred C. Roulet, Habelstr. 24, Basel, Switzerland, Secretary General.

INTERNATIONAL UNION AGAINST TUBERCULOSIS, Rio de Janeiro, Brazil, Aug. 24-27. Prof. Etienne Bernard, 66 Blvd. St. Michel, Paris 6e, France, Secretary-General.

LATIN AMERICAN CONGRESS OF PHYSICAL MEDICINE, Panama City, R. P., Feb. 24-29. Dr. Cassius Lopez de Victoria, 176 East 71st St., New York, N. Y., U. S. A., Executive Director.

NEURORADIOLOGIC SYMPOSIUM, Stockholm, Sweden, Sept. 17-20. Docent Ake Lindbom, Symposium Neuroradiologicum, Serafimerlasarettet, Stockholm K., Sweden, Secretary.

PAN-AMERICAN CONGRESS OF GASTROENTEROLOGY, Mexico City, D.F., May 11-17. Dr. R. Flores-Lopez, Calle Dr. Balmis, No. 148, Mexico City, D.F., Secretary.

PAN-EUROPEAN CONGRESS OF GASTROENTEROLOGY, Bologna, Florence and Rome, Italy, April 20-26. Prof. Guido Bassi, Policlinic of St. Orsola, Bologna, Italy, Secretary.

WORLD MEDICAL ASSOCIATION, Athens, Greece, Oct. 12-16. Dr. Louis H. Bauer, 2 East 103d St., New York 29, N. Y., Secretary General.

EXAMINATIONS AND LICENSURE

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 24-26, 1952. Sec., Dr. D. G. Gill, 537 Dexter Ave., Montgomery 4.

ALASKA: *Examination.* Juneau, March 4. Also on application in other towns where there are board members. *Reciprocity.* On application. Sec., Dr. W. M. Whitehead, Box 140, Juneau.

ARIZONA: *Examination.* Phoenix, April 15-17. *Reciprocity.* Phoenix, April 19. Sec., Dr. J. H. Patterson, 316 W. McDowell St., Phoenix.

ARKANSAS: *Examination. Regular.* Little Rock, June 5-6. Sec., Dr. Joe Verser, Harrisburg. *Homeopathic.* Little Rock, June 10-11. Sec., Dr. Carl S. Bungart, 105 N. 14th St., Fort Smith. *Eclectic.* Little Rock, June 5-6. Sec., Dr. Frank C. Smith, 2301 Broadway, Little Rock.

CALIFORNIA: *Written.* Los Angeles, Feb. 18-21; San Francisco, June 23-26; Los Angeles, Aug. 18-21; Sacramento, Oct. 20-23. Application must be received at least two weeks prior to date of examination. *Oral for Reciprocity Applicants.* San Francisco, June 21; Los Angeles, Aug. 16; San Francisco, Nov. 8. Applicants are requested not to arrange to come to an oral examination until they receive notice from the Credentials Committee. *Oral and Clinical for Foreign Medical School Graduates.* San Francisco, June 22; Los Angeles, Aug. 17; San Francisco, Nov. 9. Sec., Dr. Frederick N. Scatena, 1020 N St., Sacramento.

COLORADO: *Examination.* Denver, June 10-12. Final date for filing application is May 12. *Reciprocity.* Denver, April 8. Final date for filing application is Mar. 10. Sec., Dr. Samuel H. Brown, 831 Republic Bldg., Denver.

CONNECTICUT: *Regular Examination.* Hartford, March 11-12. Sec. to the Board, Dr. Creighton Barker, 160 St. Roman St., New Haven. *Homeopathic Examination.* Derby, March 11. Sec., Dr. Donald A. Davis, 38 Elizabeth St., Derby.

DELAWARE: Dover, July 8-10. Sec., Dr. Joseph S. McDaniel, 229 South State St., Dover.

DISTRICT OF COLUMBIA: *Reciprocity.* Washington, March 10. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Bldg., Washington.

FLORIDA: *Examination.* Jacksonville, June 29-July 1. Sec., Dr. Homer L. Pearson, 701 Dupont Bldg., Miami.

GEORGIA: Atlanta and Augusta, June. Sec., Mr. R. C. Coleman, 111 State Capital, Atlanta 3.

GUAM: The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Ex. Sec., Dr. Austin W. Matthis, Agaña.

IDAHO: Boise, July 14-16. Sec., Mr. Armand L. Bird, 305 Sun Bldg., Boise.

ILLINOIS: *Examination.* Chicago, April 1-3, June 24-26 and Oct. 7-9. Supt. of Regis., Mr. Charles F. Kervin, Capitol Bldg., Springfield.

INDIANA: Indianapolis, June 1952. Sec., Dr. Paul R. Tindall, 1138 K of P Bldg., Indianapolis 4.

IOWA: *Examination.* Iowa City, June 9-11. Sec., Dr. M. A. Royal, 506 Fleming Bldg., Des Moines.

KANSAS: Kansas City, June 4-5. Sec., Dr. O. W. Davidson, 864 New Brotherhood Bldg., Kansas City.

KENTUCKY: *Examination.* Louisville, June 4-6. Sec., Dr. Bruce Underwood, 620 S. Third St., Louisville.

MAINE: Portland, March 11-12. Sec., Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Examination.* Baltimore, June 17-20. Sec., Dr. Lewis P. Grundy, 1215 Cathedral St., Baltimore. *Homeopathic.* Baltimore, June 17-18. Sec., Dr. John A. Evans, 6029 Bellona Ave., Baltimore.

MICHIGAN: *Examination.* June. Sec., Dr. J. E. McIntyre, 100 W. Allegan St., Lansing 8.

MINNESOTA: Minneapolis, April 15-17. Sec., Dr. Julian F. DuBois, 230 Lowry Medical Arts Bldg., St. Paul 2.

MONTANA: Helena, April 1. Sec., Dr. S. A. Cooney, 214 Power Block, Helena.

NEW HAMPSHIRE: Concord, March 12-13. Sec., Dr. John S. Wheeler, State House, Concord.

NEW JERSEY: *Examination.* Trenton, June 17-20. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, April 14-15. Sec., Dr. Charles J. McGoey, Coronado Bldg., Santa Fe.

NORTH CAROLINA: *Reciprocity.* Pinehurst, May 5. *Written.* Raleigh, June 16-19; *Reciprocity.* Raleigh, June 17. Sec., Dr. Joseph J. Combs, 716 Professional Bldg., Raleigh.

NORTH DAKOTA: *Examination.* Grand Forks, July 9-11. *Reciprocity.* Grand Forks, July 12. Sec., Dr. C. J. Glaspel, Grafton.

OHIO: *Examination.* Columbus, June 17-20. *Reciprocity.* Columbus, April 1. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus 15.

OKLAHOMA: *Examination.* Oklahoma City, June 4-5. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON: *Reciprocity.* Portland, April 18-19. *Examination.* Portland, July. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland.

PUERTO RICO: *Examination.* San Juan, March 4. Sec., Mr. Luis Cueto Coll, Box 3717, Santurce.

RHODE ISLAND: *Examination.* Providence, April 3-4. Sec., Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: *Reciprocity.* Columbia, March 3 and April 7. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA: Rapid City, July 15. Sec., Dr. C. B. McVay, Yankton Clinic, Yankton.

TENNESSEE: *Examination.* Memphis, March 26-27. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis.

TEXAS: Fort Worth, June 19-21. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth.

UTAH: *Examination.* Salt Lake City, July. Asst. Dir., Mr. Frank E. Lees, 314 State Capitol Bldg., Salt Lake City 1.

VIRGINIA: *Examination.* Richmond, June 12-14. *Reciprocity.* Richmond, June 11. Sec., Dr. K. D. Graves, 631 First St., S.W., Roanoke.

VIRGIN ISLANDS: St. Thomas, June 4-5. Sec., Dr. Earle M. Rice, St. Thomas.

WEST VIRGINIA: Charleston, April 7-8. Sec., Dr. H. H. Dyer, State Office Bldg. No. 3, Charleston 5.

WASHINGTON: Seattle, July. Sec., Mr. Edward C. Dohm, Department of Licenses, Olympia.

WISCONSIN: Milwaukee, July 8-10. Sec., Dr. A. G. Koehler, 46 Washington Blvd., Oshkosh.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: *Examination.* On application. Juneau or other towns in Territory as decided by Board. *Reciprocity.* On application. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

ARIZONA: Tucson, March 18. Sec., Mr. Herbert D. Rhodes, University of Arizona, Tucson.

COLORADO: Denver, March 5-6. *Examination.* Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

DISTRICT OF COLUMBIA: *Examination.* Washington, April 21-22. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Bldg., Washington, D. C.

FLORIDA: Gainesville, June 7. *Examination.* Sec., Mr. M. W. Emmel, Box 340, University of Florida, Gainesville.

OKLAHOMA: *Examination.* Oklahoma City, April 14. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON: *Examination.* Portland, March 1, June 7, Sept. 6 and Dec. 6. Sec., Dr. Charles D. Byrne, State Board of Higher Education, University of Oregon, Eugene.

TENNESSEE: *Examination.* Memphis and Nashville, March 20-21. Sec., Dr. O. W. Hyman, 874 Union Ave., Memphis.

TEXAS: Austin, April. *Examination.* Sec., Bro. Raphael Wilson, 306 Nalle Bldg., Austin.

WISCONSIN: *Examination.* Madison, April 5, and Milwaukee, June 7. Sec., Mr. W. H. Barber, Ripon College, Ripon.

* Basic Science Certificate required.

DEATHS

Blake, Francis Gilman * New Haven, Conn., Sterling Professor of Medicine, Yale University School of Medicine, died in Walter Reed General Hospital, Washington, D. C., Feb. 1, aged 64. Dr. Blake was born in Mansfield Valley, Pa., Feb. 22, 1887. He graduated from Dartmouth College, Hanover, N. H., in 1908 and received his medical degree from Harvard Medical School, Boston, in 1913. For the next three years he was on the staff of Peter Bent Brigham Hospital in Boston as intern, assistant resident, and resident physician. In 1916 he went to the Rockefeller Institute for Medical Research for a year. From 1917 to 1919 he was assistant professor of medicine at the University of Minnesota Medical School, Minneapolis. In 1919 he returned to the Rockefeller Hospital in New York as associate in medicine, in 1920 became an associate member of the Rockefeller Institute, and from 1924 to 1935 was a member of its scientific board of directors. At the time of his appointment to the Yale University School of Medicine faculty in 1921 he was the youngest man ever to be named to a full professorship there. He was John Slade Ely Professor of Medicine from 1921 to 1927, when he became Sterling Professor of Medicine, a post he held at the time of his death. He served as dean from 1940 to 1947 and in the latter year resigned that position to devote his full time to the chairmanship of the department of internal medicine and to his work for various governmental and scientific agencies. Since Jan. 1 of this year, as civilian technical director of medical research in the office of the Army Surgeon General, Dr. Blake had served as expert consultant to the chairman of the Army Medical Research and Development Board in the evaluation of current and proposed research projects conducted by Army medical installations and 81 cooperating civilian institutions. On leave of absence from Yale, Dr. Blake retired earlier this year as chairman of the Committee on Medical Sciences of the Research and Development Board in the Office of the Secretary of Defense. He had held that post since 1948. During World War I Dr. Blake rose to the rank of major in the medical reserve corps of the U. S. Army. During World War II he served as special consultant to President Roosevelt and Secretary of War Stimson and as president of the Army Epidemiological Board. For his work as director of the Field Commission on scrub typhus in New Guinea in 1943, he received the United States Typhus Medal and in 1944 he was awarded the Medal for Merit. From 1925 to 1936 he was a member of the National Research Council, Division of Medical Sciences, and chairman from 1933 to 1936; a member of the fellowship board from 1927 to 1946, chairman of the board from 1936 to 1946; a member of the committee on chemotherapy since 1940; a member of the clinical panel on antimalarials from 1942 to 1946 and of the medical committee since 1947, and chairman of the subcommittee on infectious diseases from 1940 to 1946. For many years he was a member of the National Advisory Health Council of the U. S. Public Health Service and chairman of the advisory council of the Life Insurance Medical Research Fund. In 1932 he was a member of the executive council of the Association of American Medical Colleges. He had been chairman of the Section on the Practice of Medicine of the American Medical Association in 1937-1938; past president and vice-president of the Association of American Physicians, of which he had been recorder from 1934 to 1940 and councilor from 1941 to 1947; past president of the American Society for Clinical Investigation and American Association of Immunologists; in 1946 vice-president of the American Association for the Advancement of Science; and a fellow, from 1939 to 1947 a regent, and in 1948 vice-president of the American College of Physicians. He was a fellow of the National Academy of Sciences, a member of the American Association of Pathologists and Bacteriologists, Society of American Bacteriologists, American Society for Experimental Biology and Medicine, American Society for Experimental Pathology, Connecticut Academy of Arts and Sciences, Harvey Society, Chi Phi, Phi Rho Sigma,

Alpha Omega Alpha, and Sigma Xi. In 1939 he was a member of the executive committee of the Third International Congress of Microbiology. During the annual meeting of the Rhode Island Medical Society in 1945, Dr. Blake was awarded the Charles V. Chapin Memorial Award of the City of Providence and gave the annual Charles V. Chapin Oration before the medical society. In 1946 he received the Lasker Group Award for the Army Epidemiological Board. In 1935 he was a Harvey lecturer. Dr. Blake was certified by the American Board of Internal Medicine. Since 1921 he had been physician-in-chief of the Grace-New Haven Hospital, and was for many years vice-president of the board of scientific directors of the Yerkes Laboratories for Primate Biology. He had been prominently associated with many important developments in medical education and medical research and administration and has had a strong influence upon the modern growth of the Yale University School of Medicine. He had contributed through his research to the treatment of scarlet fever with antitoxin and to the treatment of pneumonia by serums and by sulfapyridine and its related compounds. Dr. Blake was the recipient of an honorary M.A. degree from Yale in 1921 and doctor of science degree from Dartmouth in 1936.

Trick, Harry Radley * Buffalo; born in Stafford, N. Y., April 1, 1874; University of Buffalo School of Medicine, 1901; formerly on the faculty of his alma mater; member of the House of Delegates of the American Medical Association from 1929 to 1931; past president of the Medical Society of the State of New York; active in the Erie County Medical Society, serving as chairman of its committee for revision of the constitution and bylaws in 1934 and as a member of a similar committee in 1951; in 1921 and 1922 president of the medical alumni of the University of Buffalo; fellow of the American College of Surgeons and former member of its board of governors; member of the Buffalo Surgical Society and Buffalo Academy of Medicine; for many years medical director of the Hospital Service Corporation of Western New York, known as Blue Cross; served during World War I; consulting surgeon, Wyoming County Community Hospital in Warsaw, Buffalo General, Edward J. Meyer Memorial and Buffalo State hospitals; connected with an American Red Cross mobile unit of blood banks; died in Warren (Pa.) General Hospital Dec. 19, aged 77, of coronary artery disease.

Stucky, George Courtney * Charlotte, Mich.; born in Louisville, Ky., May 10, 1888; University of Michigan Medical School, Ann Arbor, 1923; lecturer in public health practice, University of Michigan School of Public Health, Ann Arbor; certified by the American Board of Preventive Medicine in Public Health; served as president of the Michigan Health Officer's Association; past president of the Michigan Trudeau Society and Michigan Sanatorium Association; formerly a director of the National Tuberculosis Association; member of the American Trudeau Society and the American Public Health Association; served as a member of the board of trustees of the Michigan Tuberculosis Association; fellow of the American College of Physicians; director of the Eaton County Health Department; at one time associated with the W. K. Kellogg Foundation in Battle Creek; for many years superintendent and medical director of Ingham Sanatorium in Lansing; on the staff of the Hayes-Green-Beach Hospital, where he died Nov. 26, aged 62, of thrombosis of the basilar artery.

Black, Robert Alfred * Chicago; born in Clarksburg, Pa., April, 1879; Northwestern University Medical School, Chicago, 1904; professor emeritus of pediatrics at Stritch School of Medicine of Loyola University; specialist certified by the American Board of Pediatrics; past president of the Chicago Pediatric Society and member of the board of governors of the Chicago Heart Association; member of the American Academy of Pediatrics; fellow of the American College of Physicians; at one time a member of the city board of health and acting president of the board late in 1938 and early in 1939; member of the advisory board of the Municipal Contagious Disease Hospital; retired head of the pediatrics service at Mercy Hospital; honorary chi-

of staff at La Rabida Jackson Park Sanitarium, where he had been on the visiting staff; served with St. Mary of Providence School for Handicapped Girls; died in Maitland, Fla., Jan. 13, aged 72, of pneumonia.

Aaron, Charles Dettie ⊕ Detroit; born at Lockport, N. Y., May 8, 1866; University of Buffalo School of Medicine, 1891; from 1898 to 1938 professor of gastroenterology and dietetics at the Detroit College of Medicine, now a part of Wayne University College of Medicine, where he was an emeritus professor of gastroenterology; one of the founders, an honorary member, and, for many years, secretary-treasurer of the American Gastroenterological Association; an Associate Fellow of the American Medical Association; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; past president of the Detroit Academy of Medicine; author of "Diseases of Digestive Organs"; consultant in stomach diseases at Receiving and Shurly hospitals and Harper Hospital, where he died Dec. 3, aged 85, of arteriosclerosis.

Horan, Thomas Neil ⊕ Detroit; born in Detroit April 3, 1902; University of Michigan Medical School, Ann Arbor, 1926; assistant professor of clinical medicine at Wayne University College of Medicine; certified by the American Board of Internal Medicine; fellow of the American College of Physicians; served during World War II and was awarded the Bronze Star "for meritorious achievement in support of military operations"; on the staffs of Harper Hospital in Detroit and the Veterans Administration Hospital in Dearborn; in 1942 at the Atlantic City session of the American Medical Association was given honorable mention for his exhibit on laparoscopy, or intra-abdominal photography in color; died Dec. 1, aged 49, of myocardial infarction and arteriosclerotic heart disease.

Aldridge, Mahlon Roy ⊕ Jefferson City, Mo.; St. Louis College of Physicians and Surgeons, 1907; died in St. Mary's Hospital Dec. 1, aged 73, of heart disease.

Allyn, Paul R. ⊕ Waverly, Ill.; Barnes Medical College, St. Louis, 1903; city health officer; formerly mayor and member of the city council; died in Memorial Hospital, Springfield, Dec. 12, aged 72.

Arnold, Harold Sears, Woodbridge, Conn.; Yale University School of Medicine, New Haven, 1903; member of the American Medical Association; served on the faculty of his alma mater; affiliated with New Haven Hospital, where he died Dec. 20, aged 74, of pulmonary emphysema.

Baker, Frank Lawrence, Hildreth, Neb.; Lincoln Medical College of Coter University, 1910; member of the board of education from 1930 to 1933; died in Holdrege Hospital in Holdrege Oct. 28, aged 66, of coronary artery disease.

Bender, Irwin Henry ⊕ Brooklyn; Long Island College Hospital, Brooklyn, 1923; on the staff of Samaritan Hospital; died in Long Island College Hospital Dec. 18, aged 52, of cerebral hemorrhage.

Beyer, Othmar Julius, Irvington, N. J.; Medizinische Fakultät der Universität, Wien, Austria, 1915; on the staff of Irvington General Hospital, where he died Dec. 3, aged 61, of coronary occlusion.

Boemer, Irving Henry ⊕ St. Louis; St. Louis University School of Medicine, 1915; member of the International College of Surgeons; fellow of the American College of Surgeons; senior instructor in surgery at his alma mater; affiliated with St. John's Hospital, Missouri Pacific Hospital, and St. Mary's Group of Hospitals; died Dec. 3, aged 62, of cerebral infarction.

Brown, Edgar Milton, Zanesville, Ohio; Medical College of Ohio, Cincinnati, 1893; served during World War I; died in Good Samaritan Hospital Oct. 14, aged 85, of carcinoma of the kidney.

Brunner, Austin Franklin, Sharon Hill, Pa.; Jefferson Medical College of Philadelphia, 1931; member of the American Medical Association; served during World War II; president of the board of health of Sharon Hill; affiliated with Methodist Episcopal Hospital in Philadelphia and Taylor Hospital in Ridley Park; died Dec. 2, aged 44, of coronary occlusion.

Burke, Edward Francis ⊕ Providence, R. I.; Tufts College Medical School, Boston, 1918; also a graduate in pharmacy; member of the New England Obstetrical and Gynecological Society; af-

filiated with Roger Williams General Hospital and St. Joseph's Hospital, where he died Dec. 20, aged 70, of carcinoma of the bladder.

Chidlow, Alexander D. ⊕ Villa Park, Ill.; Jenner Medical College, Chicago, 1917; died in Du Page Memorial Hospital, Elmhurst, December 3, aged 72, of cerebral thrombosis.

Diefenderfer, Harold, Chicago; University of Pennsylvania Department of Medicine, Philadelphia, 1894; died Jan. 1, aged 82, of sclerotic myocarditis.

Dillon, John Alfred, Larned, Kan.; Kansas Medical College, Topeka, 1893; also a graduate in dentistry; member of the American Medical Association and in 1929 member of its House of Delegates; past president of the Kansas Medical Society; fellow of the American College of Surgeons; served as lecturer in psychiatry at the University of Kansas School of Medicine in Kansas City; superintendent of the Larned State Hospital from 1928 to 1945; died Dec. 3, aged 78, of cerebral hemorrhage.

Dittmer, Samuel Edward ⊕ Kouts, Ind.; Hahnemann Medical College and Hospital, Chicago, 1911; served during World War I; physician and surgeon for the Erie Railroad; on the staff of Porter Memorial Hospital in Valparaiso, where he died Dec. 1, aged 66, of myocardial infarction.

Dougherty, James J., Avoca, Pa.; Jefferson Medical College of Philadelphia, 1908; member of the American Medical Association; served on the staffs of Taylor Hospital in Taylor, St. Mary's Hospital in Scranton, and Pittston (Pa.) Hospital; died Nov. 12, aged 70, of bronchopneumonia.

Fava, Philip Vincent, Newark, N. J.; Tufts College Medical School, Boston, 1924; fellow of the American College of Surgeons; attending gynecologist, Newark City Hospital; on the courtesy staffs of Presbyterian, St. James, Lutheran, and St. Michael's hospitals in Newark and St. Mary's Hospital in Orange; died Dec. 5, aged 54, of carcinoma of the transverse colon.

Fletcher, Benjamin Kennard, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1895; for many years professor of pediatrics at his alma mater; died in Hahnemann Hospital Dec. 17, aged 83, of carcinoma of the prostate.

Graves, Waldo Neil, Duluth, Minn.; Rush Medical College, Chicago, 1924; member of the American Medical Association; fellow of the American College of Surgeons; served during World Wars I and II; on the staffs of Miller Hospital, St. Mary's Hospital, and St. Luke's Hospital, where he died Dec. 5, aged 53, of carcinoma of the lung.

Handley, Walter Edward, Springfield, Mo.; Barnes Medical College, St. Louis, 1906; member of the American Medical Association; commissioner of health and sanitation; on the courtesy staff of Burge Hospital; died Nov. 26, aged 74, of acute coronary thrombosis.

Henderson, Edward Emmett ⊕ Columbus, Kan.; University of Kansas School of Medicine, Kansas City, 1907; died Nov. 5, aged 84, of cerebral hemorrhage.

Hilborn, Robert Ross, Polkton, N. C.; American Medical Missionary College, Battle Creek, Mich., and Chicago, 1904; Cleveland Homeopathic Medical College, 1908; formerly a medical missionary in North Africa; died Nov. 14, aged 71.

Hughes, James Thomas, Fountain Run, Ky.; University of Tennessee Medical Department, Nashville, 1898; died Dec. 22, aged 77.

Jackson, Carl A. ⊕ Kansas City, Mo.; University Medical College of Kansas City, 1897; an Associate Fellow of the American Medical Association; veteran of the Spanish-American War; on the staff of Trinity Lutheran Hospital, where he died Nov. 27, aged 74, of coronary occlusion.

Jacob, David, Springfield, Ill.; Universität Basel Medizinische Fakultät, Switzerland, 1936; member of the American Medical Association; served during World War II; died Oct. 3, aged 42, in an automobile accident.

Maloy, Daniel W. F., Milan, Ga.; Hospital Medical College, Atlanta, 1911; member of the American Medical Association; died Oct. 31, aged 61.

Montgomery, Enoch Albert, Unionville, Mo.; Barnes Medical College, St. Louis, 1899; member of the American Medical Association; past president of the North Central Counties Medical Society; died recently, aged 80, of carcinoma of the prostate.

Moore, Grover Cleveland ☉ Ponca City, Okla.; University of Arkansas School of Medicine, Little Rock, 1913; past president and secretary of Kay County Medical Society; on the staff of Ponca City Hospital; died Nov. 18, aged 64, of a heart disease.

Peters, William Chute, Bangor, Maine; born June 15, 1868; Tufts College Medical School, Boston, 1902; member of the American Medical Association and New England Surgical Society; fellow of the American College of Surgeons; past president of the Bangor Anti-Tuberculosis Association and the Maine Tuberculosis Association; served during World War I; at one time on the faculty of his alma mater as an assistant in microscopic anatomy and instructor in operative surgery; consulting surgeon, Eastern Maine General Hospital; died recently, aged 83.

Prince, Russell Warren ☉ San Bernardino, Calif.; California Eclectic Medical College, Los Angeles, 1916; on the staff of the San Bernardino Community Hospital; died Nov. 27, aged 60, of acute coronary thrombosis.

Radzow, Karl Herbert, Fontana, Calif.; Western Reserve University School of Medicine, Cleveland, 1943; member of the American Medical Association; interned at the City Hospital in Cleveland, where he subsequently held a residency in obstetrics and gynecology and was chief resident in obstetrics and gynecology; formerly resident in obstetrics and gynecology at the University Hospital in Cleveland; served during World War II; joined the staff of the Kaiser Fontana Hospital Association in July, 1950; killed Nov. 28, aged 34, in a car accident.

Roberts, Oscar Harvey, Bethel, Ky.; Kentucky School of Medicine, Louisville, 1898; died in Mount Sterling Nov. 6, aged 78, of uremia and carcinoma of the prostate.

Romig, Joseph Herman ☉ Colorado Springs, Colo.; Hahnemann Medical College and Hospital of Philadelphia, 1896; an ordained minister; fellow of the American College of Surgeons; member of the Alaska Territorial Medical Association; served for many years as medical missionary for the Moravian Missions of Alaska and at one time as mayor of Anchorage; died Nov. 23, aged 79.

ss, Edward Smithers, Darby, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1920; died Nov. 19, aged 55.

Schmaltz, Walter Franklin, Dallas, Texas; Lincoln Medical College of Cotner University, 1910; specialist certified by the American Board of Otolaryngology; served during World War I; lieutenant colonel, retired, medical reserve corps, U. S. Army; formerly affiliated with the Veterans Administration hospitals in Waco and Dallas; died Oct. 15, aged 67, of paralysis agitans.

Schulz, Clarence Henry ☉ La Grange, Ind.; Indiana University School of Medicine, Indianapolis, 1926; on the staff of La Grange County Hospital; died November 17, aged 50.

Scorpio, Angelo ☉ Providence, R. I.; Harvard Medical School, Boston, 1927; affiliated with Rhode Island Hospital in Providence and State Infirmary in Howard; died November 14, aged 55, of acute coronary thrombosis.

Scott, Stuart L., Staunton, Va.; Meharry Medical College, Nashville, Tenn., 1905; died November 11, aged 71, of coronary thrombosis.

Sharkey, William Patrick ☉ Portland, Ore.; University of Oregon Medical School, Portland, 1926; past president of the Portland Society of Obstetrics and Gynecology; served during World Wars I and II; affiliated with St. Vincent's and Providence hospitals; died November 16, aged 51, of heart disease.

Shearer, Henry Jackson, Altheimer, Ark. (licensed in Arkansas in 1907); died in Davis Hospital, Pine Bluff, Nov. 9, aged 81, of cardiac failure with complete heart block.

Sherman, Warren Hunter ☉ Lowell, Mass.; Medical School of Maine, Portland, 1905; an Associate Fellow of the American Medical Association; member of the New England Pediatric Society; on the staff of Lowell General and St. John's hospitals; died Nov. 9, aged 73, of cerebral hemorrhage and generalized arteriosclerosis.

Short, James Edward, Buffalo; University of Buffalo School of Medicine, 1911; member of the American Medical Association; served during World War I; for many years on the staff of the Edward J. Meyer Memorial Hospital; died in Millard Fillmore Hospital November 26, aged 64, of coronary occlusion.

Simmons, Hugh Ludwig ☉ Worcester, Mass.; Tufts College Medical School, Boston, 1916; served during World War I; a captain in the medical reserve corps of the U. S. Army from 1923 to 1933; appointed to the obstetrical service at Worcester City Hospital in 1919, serving for the past 17 years as one of four senior obstetricians; president of the Worcester City Hospital Staff Association; member of the Association of Military Surgeons of the United States; died Nov. 20, aged 58.

Smith, David S., Utica, Miss.; Memphis (Tenn.) Hospital Medical College, 1912; died in Lutheran Hospital, Vicksburg, November 30, aged 69, of bronchogenic carcinoma.

Smith, Harry Anthony ☉ Huntington, W. Va.; Medical College of Virginia, Richmond, 1934; formerly practiced in Wheeling, where he was city and county health officer; while in Wheeling he was president and secretary of the Boone County Medical Society and on the staff of the Madison General Hospital; attached to the Veterans Administration Regional Office; died December 8, aged 59, of coronary occlusion.

Sperling, Samuel N., Venice, Calif.; Northwestern University Medical School, Chicago, 1927; died Nov. 10, aged 57, of coronary occlusion.

Stark, Ernest Hanie, Paris, Texas; Vanderbilt University School of Medicine, Nashville, Tenn., 1900; past president of the Lamar County Medical Society; served in France during World War I; died recently, aged 77, as the result of a cerebral hemorrhage suffered three years ago.

Stevenson, Onnie Earle ☉ Parsons, Kan.; University of Kansas School of Medicine, Kansas City, 1911; formerly county health officer; served as superintendent of State Hospital for Epileptic; died in Menorah Hospital in Kansas City, Mo., Nov. 13, aged 6.

Stillger, Walter Francis ☉ Hicksville, N. Y.; University at Bellevue Hospital Medical College, New York, 1915; served during World War I; surgeon for the fire department of Hicksville for many years health officer for the town of Oyster Bay; on the staffs of Meadowbrook Hospital in Hempstead and Nassau Hospital in Mineola; died Nov. 10, aged 60, of cerebral hemorrhage, hypertensive cardiovascular heart disease, and chronic glomerulonephritis.

Stookey, Walter M. ☉ Salt Lake City; Marion-Sims College of Medicine, St. Louis, 1898; died November 19, aged 82.

Sudler, Wright S., Baltimore; College of Physicians and Surgeons, Baltimore, 1903; formerly county coroner; died in Towson, Md., November 19, aged 72.

Swinford, Charles Lewis, Cynthia, Ky.; Hospital College of Medicine, Louisville, 1906; died Nov. 24, aged 66, of cerebral hemorrhage.

Thompson, Louis Levi, Reading, Pa.; Jefferson Medical College of Philadelphia, 1896; died November 28, aged 76, of gangrene of the foot.

Thomson, Robert Strachan ☉ Fitchburg, Mass.; Harvard Medical School, Boston, 1938; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; affiliated with Hospital Cottages for Children in Baldwinville and Burbank Hospital; died in Evanston, Wyo., November 19, aged 39, in a Union Pacific train accident.

Warren, Melvin George Edward, Seattle; McGill University Faculty of Medicine, Montreal, Canada, 1939; member of the American Medical Association; affiliated with Seattle General and Doctors hospitals; drowned off Orcas Island Nov. 1, aged 42.

CORRECTION

In the obituary of Dr. Dallas Burton Phemister (THE JOURNAL, Jan. 19, page 216) it was incorrectly stated that Dr. Phemister was a vice-president of the International College of Surgeons. He was a vice-president of the International Society of Surgeons.

GOVERNMENT SERVICES

ARMY

Symposium on Trauma.—A symposium on the treatment of trauma in the armed forces will be conducted at the Walter Reed Army Medical Center, Washington, D. C., March 10-12. Sponsored jointly by the Division of Medical Sciences of the National Research Council and the Army Medical Service Graduate School, the symposium is designed to review the problems of trauma in military medicine. Scheduled for discussion are medical organization for handling of trauma in military campaigns and civil disasters, emergency treatment of the wounded, surgical problems related to traumatic injury, rehabilitation of battle casualties, complications related to traumatic injury, and research in military medicine. National and international authorities in these fields will appear on the various programs.

Physicians eligible to attend the symposium include medical officers of the armed forces on active duty, with the exception of those enrolled in the residency training program; full-time civil service physicians on duty at Army installations, physicians and surgeons from other federal agencies, and civilian physicians and surgeons. Army medical officers and civil service physicians at Army installations should make application through the commander of their installation. Applications of other armed forces medical officers should be forwarded through regularly established channels. Applications for all other interested physicians should be forwarded directly to the Commanding General, Walter Reed Army Medical Center, Washington 12, D. C. Applications must reach the commandant of the graduate school by March 1, 1952.

Captain Pocock Awarded the Bronze Star.—Capt. Donald G. Pocock, MC, now assistant professor of military science and tactics at Vanderbilt University, was presented with the Bronze Star medal Jan. 25 for meritorious service in Korea as surgeon of the 96th Field Artillery Battalion. Presentation was made by Col. Robert H. Elliott, professor of military science and tactics at Vanderbilt, in the presence of members of his staff, Tennessee Military District officers, university officials, and friends. Captain Pocock is on the military science and tactics staff for the School of Medicine ROTC Detachment at Vanderbilt.

PUBLIC HEALTH SERVICE

Regular Corps Examination for Medical Officers.—A competitive examination for appointment of medical officers to the regular corps of the Public Health Service will be held on June 3-5 at a number of points throughout the United States. Applications must be received no later than April 30, 1952.

The regular corps is a commissioned officer corps composed of members of various medical and scientific professions, appointed in appropriate categories such as medicine, dentistry, nursing, engineering, and pharmacy. Appointments will be made in the grades of assistant surgeon and senior assistant surgeon. In making assignments, consideration is given to the officer's preference, ability, and experience; however, all commissioned officers are subject to change of station and assignment as necessitated by the needs of the service. Appointments are permanent in nature and provide opportunities to qualified physicians for a life career in clinical medicine, research, and public health. To be eligible for either grade, candidates must be a United States citizen, at least 21 years of age, and a graduate of a recognized school of medicine. The grade of assistant surgeon requires at least seven years of educational training and professional experience subsequent to high school. The grade of senior assistant surgeon requires at least 10 years of educational training and professional experience subsequent to high school.

Applicants who will meet these qualifications within nine months of the date of the written examination will be admitted, but may not be appointed until they fulfill the requirements.

Physicians who are successful in the examination and are now serving internships will not be placed on active duty in the regular corps until completion of internship. The examination will include an oral interview, physical examination, and written objective tests covering the professional field. Gross pay is identical to that of officers of equivalent rank in the Army and Navy. Entrance pay for an assistant surgeon with dependents is \$5,686.56 per annum; for senior assistant surgeon with dependents, \$6,546. These figures include the \$1,200 annual additional pay received by medical officers as well as subsistence and rental allowance. Officers on active duty are not eligible to receive disability compensation from the Veterans Administration. Provisions are made for promotion at regular intervals up to and including the grade of senior surgeon (commander) and for promotion by selection to the grade of medical director (captain). Retirement pay after 30 years of service or at the age of 64 is three-fourths of annual basic pay at the time of retirement. Information may be obtained by writing to the Surgeon General, United States Public Health Service, Washington 25, D. C. Attention: Division of Commissioned Officers.

VETERANS ADMINISTRATION

Seminars on Modern Concepts in Psychiatry.—The Veterans Administration Regional Office at 366 West Adams St., Chicago, and the Veterans Administration Hospital at Downey, Ill., five miles south of Waukegan, Ill., have been sponsoring a series of weekly seminars on modern concepts in psychiatry. The seminars will continue until May 28. The speakers and their subjects for the remaining program will be as follows:

On March 18—Dr. Harry C. Solomon, professor of psychiatry, Harvard University Medical School, Boston, will speak on "The Acute Psychoses" at 10 a. m. and 1 p. m. at Downey and at 8 p. m. at the Chicago Regional Office in a joint meeting with the Illinois Psychiatric Society.

On March 26—Dr. Paul H. Hoch, assistant professor of psychiatry, Columbia University College of Physicians and Surgeons, New York, at 10 a. m. and at 1 p. m. at Downey on "The Pseudoneurotic Form of Schizophrenia" and at 8 p. m. at the Chicago Regional Office on "Theoretical and Clinical Aspects of Anxiety."

On April 2—Dr. Harold E. Himwich, director, Research Division, State Research Hospital, Galesburg, Ill., will speak at 10 a. m. and 1 p. m. at Downey on "Functional Organization of the Brain" and at 8 p. m. at the Chicago Regional Office on "Experimental Epilepsy."

On April 8—Dr. L. J. Meduna, professor of psychiatry, University of Illinois College of Medicine, will speak at the Chicago Regional Office at 8 p. m. on "Schizophrenia and Schizophreniform States."

On April 30—Dr. R. B. Suitt, associate in neuropsychiatry, Duke University School of Medicine, Durham, N. C., will speak at 10 a. m. and 1 p. m. at Downey on "Changes in Dart Test Performance Brought About by Prefrontal Leucotomy" and at 8 p. m. at the Chicago Regional Office on "Manifestations of Depression."

On May 7—Dr. Karl M. Bowman, professor of psychiatry, University of California Medical School, will speak at 10 a. m. and 1 p. m. at Downey on "The Problem of Homosexuality" and at the Chicago Regional Office at 8 p. m. on "Children Brought Before the Juvenile Court in Connection with Sex Offenses."

On May 21—Dr. David M. Rioch, technical director, Neuro-Psychiatry Division, Army Medical Service Graduate School, Washington, D. C., will speak at Downey at 10 a. m. and 1 p. m. on "Functions of the Mid-brain" and at the Chicago Regional Office at 8 p. m. on "The Need for an Operational Terminology in Psychiatry."

On May 28—Dr. Henry A. Davidson, of the Veterans Administration, will speak on "Scientific Article Writing" at 10 and 11 a. m. and 1 p. m. at Downey.

Residencies in Psychiatry.—The Veterans Administration Hospital, Lyons, N. J., has available residencies in psychiatry for one to three years that are fully accredited by the American Board of Psychiatry and Neurology. The training can begin at any time in a program of lectures, conferences, and seminars under the direction of the Department of Psychiatry, New York Medical College, and intensive training, both intramurally and through rotation in special hospitals in the adjacent area. There is, in addition, an extensive series by guest lecturers and authorities in neurology, psychiatry and related fields as well as an annual institute at the hospital.

FOREIGN LETTERS

GERMANY

Meeting of the German Society for Research on Circulation.—The 17th meeting of the German Society for Research on Circulation was held from March 30 to April 1. A total of 700 physicians and scientists from most of the European countries participated in the meeting held in the W. G. Kerckhoff Institute in Bad-Nauheim.

Under the chairmanship of Professor Wollheim of Würzburg, the meeting opened with the subject Pulmonary Circulation. W. Forssmann of Bad-Kreuznach, who was first to undertake catheterization of the heart, described his self-experimentation of 21 years ago. U. von Euler of Stockholm and von Hayek of Würzburg described the physiology and functional anatomy, respectively, of the pulmonary blood passages. Grosse-Brockhoff of Bonn discussed the hemodynamics of the pulmonary circulation. Grosse-Brockhoff is regarded in Germany as an expert in the evaluation of congenital anomalies of the heart; he advised caution in the use of catheterization. He felt that this method is not without danger and should be used only if diagnosis or treatment demand it and in collaboration with surgical clinics. Bolt and Knipping of Cologne reported their observations on pressure in the pulmonary artery before and after lobar pneumonectomy. They observed temporary increases in pressure after the operation. In emphysema, chronic tuberculosis, and insufficiency of the left side of the heart with stasis, pressures up to 90 mm. of mercury were noted.

On the second day, von Derra of Düsseldorf summarized his results in operations on the heart. The surgical mortality of patients with patent ductus botalli has considerably improved and is now between 0 and 10%. Tetralogy of Fallot accounts for 70% of the cases of permanent cyanosis after the third year of life. The surgical mortality of 15 to 17% is justified, in view of the hopelessness of the defect if left untreated. Valvulotomy in mitral stenosis produces considerable improvement; however, its mortality is still high.

in of Basel discussed the pharmacology and Bernsmeier Esser of Düsseldorf and Stübinger of Bielefeld the clinical obtained with a ganglion blocking agent, pendiomid[®], n,n'-n'-3-pentamethyl-N,N'-diethyl-3-aza-pentane-1, 5-diammonium dibromide) in hypertension. It has been helpful also in asthma and migraine.

The third day was devoted to peripheral circulation. Hasse of Halle demonstrated that disease of the pelvic arteries with vascular obstruction can be diagnosed by clinical methods of examination, such as the walking test, the posture test, measurement of skin temperatures, and palpation of the arteries on the abdomen and in the inguinal flexure. He stressed the value of this direct diagnostic method and advised that aortography and arteriography be used only to determine the exact location and extent of vascular closures before surgical intervention, since these are not entirely harmless interventions.

ISRAEL

Revision of Law Governing Licensing of Physicians.—Revision of the present law governing the licensing of physicians is under the joint consideration of the ministries of health and justice. Dating from the days of the British mandate, the present law permits the licensing of anyone who can "satisfy the Director of the Health Department [now the Minister of Health] that he has studied medicine for not less than five years at a recognized University or Medical School and has obtained a diploma." The main revision contemplated is that immigrant physicians who are unable to prove that they have served a year's internship abroad will be required to do so before being licensed. The value

of a physician's diploma varies according to the country in which it was issued; in some countries the diploma is awarded after a year's internship and in others, without this training. Graduates of Hebrew University's Hadassah Medical School are required to intern for a year before receiving the diploma.

According to the bill now in preparation, a diploma issued after a year's internship will be deemed sufficient. More drastic changes, such as the setting up of qualifying examinations for candidates for licenses, are not contemplated. The applicant will not be examined on his skill, linguistic ability, or physical fitness; the license granted will be valid indefinitely. One reason for the government's hesitation in making regulations more rigid is the possible deterrent effect on immigration of physicians, especially from the Anglo-Saxon countries. This contingency might, however, be forestalled by granting exemptions to physicians invited to immigrate. Since the establishment of the state, 1,228 licenses have been issued, and in only 24 cases, in which the validity of the diploma was in question, were applications rejected.

Owing to mass immigration, the number of physicians has decreased from 1 for every 260 persons in 1947 to 1 for every 450 persons in 1951. This rate is still twice as high as that for England, which has 1 physician for every 900 persons. However, 45.4% of Israel's physicians are over 50 years old with only 11.2% below 35, as compared with 25% below 35 in the United States. The average age of Israel's physicians is 47. While there is no shortage of physicians in urban areas, the lack is felt in rural settlements. With the exception of the authority to draft physicians into the armed service, the government today has no power to compel physicians to work in specific locations. The Israel Medical Association constantly fought arbitrary restriction of the number of practicing physicians by the Mandatory Health Commissioner, who was empowered to fix an annual quota. The effect of this restriction was to prevent many eminently qualified physicians from following their profession. However, the association today feels that the prevailing official policy is too liberal. It is, accordingly, preparing a proposal that would give the medical association a decisive voice in ruling on each application. A candidate thus refused a license would be able to appeal to the Ministry of Health.

Roentgenography in Amebiasis and Heart Disease.—Prompted by the fact that Israel is in an endemic area for amebiasis, the roentgenography department of Hadassah University Hospital, Jerusalem, began studying, in 1943, the roentgenologic manifestations of amebiasis of the colon, liver, and chest. Some of the observations made have been summarized by Drs. A. Druckmann and S. Schorr, who divided the roentgenographic manifestations of amebiasis of the colon into two types: the diffuse type that is roentgenologically not characteristic and the localized type that is characterized by the length of the colon that is occupied by the filling defect. The lesion is often multiple and the narrowing of the lumen is incomplete. It was learned that absence of pain during the barium enema is of diagnostic significance. Antamebic treatment in some cases heals the lesion. In October, 1951, S. Schorr and A. Schwartz published another roentgenologic observation in "Amebiasis of the Liver with Concomitant Findings in the Chest." The roentgenologic manifestations of amebiasis in the liver and thorax, as observed in a series of 49 cases of proved amebiasis, are described. The first changes are limited to enlargement of the liver shadow and restriction of motility and elevation of the right leaf of the diaphragm. Other signs worth noting are localized bulging of the diaphragm on the right side, obliteration of the costophrenic or cardiophrenic angles, pleural effusion, and pneumonic consolidation with or without abscess formation. The authors point out another sign worthy of further investigation: a linear string like perpendicular shadow in the right lower lung field in ad-

dition to a fixed and deformed diaphragm. Amebiasis should always be considered in the diagnosis of pathologic conditions in the right side of the chest (pleurisy, empyema, pulmonary abscess, and basal pneumonia), especially in localities in which the disease is endemic.

During the study of the roentgenologic manifestations of the heart, a method of detecting early enlargement of the left atrium was found and was described in a paper entitled "The Recumbent Esophagogram." The authors (S. Schorr and others) reported that with the use of the esophagogram made with the patient recumbent, discrepancies between clinical and roentgenographic detection of early mitral stenosis may be considerably reduced. In view of the satisfactory results obtained, they advocate wider use of this method.

New Hebrew University-Hadassah Medical Center.—A considerable part of the \$7,500,000 needed for the erection of the Hebrew University-Hadassah Medical Center in Jerusalem has already been raised, and construction is expected to begin this year. This was reported by Dr. Kalman Mann, newly appointed director general of the Hadassah Medical Organization, at a press conference in Jerusalem. He also announced that, in accordance with the organization's policy of transferring administration of hospitals to local authorities as soon as feasible, a large part of Hadassah's preventive medicine and school hygiene services would be transferred to the Ministry of Health. He reported that 40 preventive medicine stations in Jerusalem and the corridor will be maintained and will serve about 200,000 persons. During the next two or three years basic changes will be introduced into the work of the stations providing prenatal and postnatal care. Some of them will be converted into community health centers, where stress will be placed on health instead of on illness.

The second group of medical students have finished their final examination and are now able to begin their practical work in various hospitals of the country. There were 24 students in this group, all ex-soldiers. Most of them began their medical education abroad and interrupted their studies to join the Israel Defense Forces. After cessation of fighting they were admitted to the medical school. Eighty-seven students have completed their studies at the Hadassah Medical School in Jerusalem since 1950.

Medical Teaching Mission in Israel.—During the months of September and October, 1951, a medical teaching mission operated in Israel on behalf of the World Health Organization and the Unitarian Service Committee. The members of the mission were specialists in the various branches of medical activity. The clinical and preclinical sciences and sanitary engineering were represented. The work of the mission was planned by Dr. Erwin Kohn of Geneva, together with an Israeli preparatory committee. The clinical group visited various hospitals, where they participated in conferences, lectures, and informal discussions with their Israeli colleagues. The preclinical group joined the clinicians in some of the conferences and, in addition, spent considerable time in teaching activities at the Rehovot Institute of Research and the Hebrew University. The public health group studied Israel's various health problems, and held a number of seminars on public health problems.

The mission was a great success, and the work of the public health group proved especially valuable. Israel, at present, is absorbing large numbers of immigrants from various parts of the world having widely varying standards of living. The health problems raised by this mass immigration are enormous, and the advice and guidance of these eminent experts were invaluable contributions toward their solution. The public health group has also contributed toward the long-term health policy of this country by pointing out the dangerous lack of a centralized coordinated plan in the present system in which a number of institutions independently engage in health activities. Dr. Karl Evang, in a farewell address, stated that, in matters of public health, this country is "walking on the edge of a volcano." He issued a plea, on behalf of his colleagues, for coordination and unification of health activities under a centralized authority.

Seventh Israel Pediatric Congress.—The Seventh Israel Pediatric Congress took place in Jerusalem from Dec. 12 to 14, 1951. The main subject of discussion was the condition of the immigrant child. The infant mortality rate for the Jewish population in Palestine in 1947 was 28 in 1,000 births and was among the lowest in the world. The wave of immigrants from primitive countries in Asia and Africa has caused an increase in the mortality and morbidity rates for the new state and has created gigantic problems of an administrative and medical nature for the health authorities. Tuberculosis and skin and eye diseases, widely spread among children of new immigrants, were discussed in lectures. A heavy epidemic of infantile paralysis in 1950, and to a lesser degree in 1951, has aroused great interest and concern about this disease in Israel, which before was almost free of it, except for a few sporadic cases. The epidemiology of this disease and the follow-up of cases in Israel, as well as recent progress in virus research and orthopedic problems, were covered in a second series of lectures. A third group of lectures concerned diagnosis and surgical treatment of congenital heart disease and the experience of local physicians in this field. Another topic of lectures and discussions was prematurity, which also constitutes a major problem of the new state, because of the unusually high number of prematurely born infants and the almost complete lack of special facilities for their care. Related questions of nutrition were discussed, and the need for special stations, personnel, and facilities for transportation were pointed out.

Hysterosalpingography.—For many years, hysterosalpingography has been the subject of special investigation in Hadassah's roentgenography department. Observations made in this field were recently published in a paper entitled "Uterovenous and Uterolymphatic Intravasation in Hysterosalpingography," (A. Druckmann and A. Rozyn). Two distinct phenomena, intravasation and lymphatic transfer, were studied. Lymphatic transfer is characterized by closely reticular turbidity in the uterine wall, slow clearance of oil from the uterine body, accumulation of oil in the regional lymph nodes, and retention of iodized oil (lipiodol®) in the glands for months and even years.

PARIS

Use of Vitamin B₁₂ in Neurology.—At the Nov. 16, 1951, meeting of the Medical Society of the Paris Hospitals, Drs. J. Lereboullet and R. Pluvinage reported on the use of vitamin B₁₂ in the treatment of 74 patients with neurological disease. In 10 of 43 patients with multiple sclerosis, there were no positive reactions; in 16 patients with advanced cases, there were 4 instances of only subjective improvement. In 17 patients with cases of average intensity, there was noticeable improvement, and, in 4 instances, the patients were able to resume their normal occupations after years of illness and failure of all previous treatment. In eight patients with spastic paraplegia, including two cases of unknown origin and two cases that occurred after serious accidents, functional improvement was observed. In six out of eight patients with spinocerebellar syndromes of the acromegaly type, functional improvement and a diminution of ataxia were noted; four patients, formerly invalids, were able to resume their former activities. In two children with cerebellar atrophy, vitamin B₁₂ brought about an ambulatory state and a considerable diminution of objective cerebellar signs. In seven patients with polyneuritis, including three with Korsakoff's psychosis, results were spectacular; the three patients with Korsakoff psychosis were cured within one week. The authors believe that vitamin B₁₂ has a positive action on early polyneuritis but has no effect on old lesions. In regard to the mechanism of action of vitamin B₁₂, the authors consider two hypotheses. The first is that vitamin B₁₂ acts on myelinic elements, especially in neuroanemic syndromes and in certain cases of multiple sclerosis, in which demyelination, with comparative conservation of axons, occurs. The second hypothesis assumes an occasional direct stimulation of functions of the elements not destroyed.

CORRESPONDENCE

CHARACTER OF STUDENT AMERICAN MEDICAL ASSOCIATION

To the Editor:—"What sort of men are coming up in our ranks?" This question must occasionally come to the physician's mind as the years since his entry into practice slip by. Only a fraction of American physicians can witness the education of the next generation of practitioners. Many doctors work with interns and residents in community hospitals, but a considerable number do not encounter the profession's recruits until there is a new arrival in town or conversations occur at meetings. With the present concern over the moral fiber of youth and reports of disturbing influences on university students, it is reasonable to wonder about the men and women we are training to succeed us in times of social and economic challenge.

Those who are engaged in the tasks of medical education are spared the fears of the general public. Medical students in general have already faced the major postadolescent crises and temptations. They are a carefully selected group who have passed high admission standards that attempt to determine more about an applicant than his academic qualifications. Most medical students have idealistic motivations, whether obvious or latent. These are nurtured in medical school by the principles and the living precept of their elders. Medical schools are dedicated to train men and women to give of their skill for the good in life. As a result of knowing their students well, medical professors come to have faith in them, but recently a new development gives additional justification for that faith. The birth and rapid progress in infancy of the Student American Medical Association is a clear indication of the character of those who follow us. I have had close relations with this new group in its formative first year on local and national levels, and I believe that an impression of its potentialities may be of interest.

The Student American Medical Association has, in one year, come to be the definitive group of the student part of the profession. Despite the need for such a group, previous attempts at a union of medical students failed, because they were either ill-founded or poorly motivated. This time, however, the student founders, representing certain midwestern schools, appealed to the representative body of American medicine for counsel and were supported by instant encouragement from students at leading institutions across the country. Sympathetic support was received from the American Medical Association, and the students found their cause expedited by its instant financial aid and widespread services. This has given the student organization cause for both gratitude and moments of chagrin. Although the new association was propelled into more rapid growth and efficient organization than it might otherwise have enjoyed, this aid gave the strongly individualistic American medical students reason to wonder if the new student group was not to be but a "student front" or a "tool of the senior A. M. A.," as they put it. The relations of the American Medical Association to the student group, as expressed by the former and present executive secretaries, have dispelled these fears. Members may be proud of both the response and the attitude of the A. M. A. The participants from the headquarters staff deserve commendation for making possible effective paternal aid without extreme attachment on the one hand or direction on the other.

Finding that they have a completely student organization, the members set about to make effective contributions while in training. In times of need hitherto unknown, men have suddenly appeared from obscurity to assume leadership of the nation. So have responsible young men and women come from all parts of the country to lead this Association. I recently attended the meeting of the Student House of Delegates. Here I found practical committee members, planners with vision, energetic workers, and even skilled parliamentarians and public speakers. It was gratifying to detect the high degree of knowledge of social, political, and economic trends they possess. It was a pleasant, but not unexpected, surprise to witness the ease with which the dissector or clinical clerk dons the toga and works as a man among men.

The House of Delegates of the Student American Medical Association is a virile, progressive group. Despite their wide geographical origins, the delegates reflect a favorable harmony of thought and the universal nature of student problems. The proceedings of the House of Delegates revealed several important features of the Association's character: a democratic willingness for all to be heard amidst the careful discussion of matters before them; a reluctance to act definitively without thorough investigation; a desire to cooperate with other agencies involved in similar problems of internship selection, selective service, and curricular matters; and cautious reluctance to affiliate with international student professional groups until their aims and programs could be ascertained. Their major theme is one of careful building of long-range programs while working toward certain immediate objectives. Youth is often rebellious and impulsive, but this organization already shows the good judgment and desire to cooperate that one expects with maturity.

It is natural to wonder about the attitude of American medical students toward the future character of medical practice. By acting to support the American Medical Foundation by resolution and by planning a financial contribution from their treasury, the House of Delegates of the Student American Medical Association clearly showed that they are devoted to the medical profession in its historic form of practice as a free and independent enterprise. We occasionally hear of students who feel that governmental control of medicine would be a desirable objective. In the Student American Medical Association there is no indication that any large numbers of our students hold such convictions.

These observations indicate the character of the Student American Medical Association to be one of serious consideration of future obligations as practitioners and citizens. The colleges have trained our students well; the medical schools are developing their skills and molding favorable philosophies. The Student A. M. A. provides them with a long-needed voice and an opportunity to prove that they are well worthy to assume full stature as our colleagues at the appointed time.

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DIAGNOSIS OF MACULAR LEPROSY

To the Editor:—In regard to the article on the diagnosis of leprosy by Dr. Robert K. Maddock, in *THE JOURNAL* for Jan. 5, 1952 (page 44), I would like to say that for a few years following 1895 my father, Dr. Luis F. Alvarez, was in charge of research in leprosy in Hawaii. After studying at Johns Hopkins, he returned to Honolulu and built up a board of health research laboratory at Kalihi. There he worked for several years trying to find a remedy for leprosy.

He soon devised a method that was highly successful in the diagnosis of the macular form of the disease. With a fine mouse-tooth forceps he would raise a tiny bit of the skin in a suspicious patch and snip it off with sharp scissors. He would drop this into a small mortar with a few drops of water, and, as a boy, it was my job to grind it for a few minutes until it disappeared. The few drops of liquid were then dried on a slide and stained in the usual way with carbolfuchsin. Commonly the acid-fast bacilli were found, and my father came to depend greatly on the test. Unfortunately, he reported it (as I remember) only at the World Leprosy Conference held in Berlin in 1897, and hence only the leprologists of that time knew of it. Several used it and liked it. I imagine it would be well to use it again, because it was such a simple and successful procedure.

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BUREAU OF LEGAL MEDICINE AND LEGISLATION

MEDICOLEGAL ABSTRACTS

Chiropractors: Rupture of Brain Tumor Following Adjustment.—The plaintiff sued for damages alleged to have been caused by the malpractice of the defendant chiropractor. From a judgment in favor of the plaintiff, the defendant appealed to the Supreme Court of Montana.

The plaintiff was suffering from a stiff neck, headache and sore spot behind the right ear and went to the defendant's office for relief. He took an x-ray of the plaintiff's neck and said that the picture showed that two vertebrae were out of place, and he recommended a series of adjustments to return such vertebrae to their proper position in the spine. The plaintiff testified that on the date of one of these adjustments she got on the table in the defendant's office. "As soon as I was in the right position the thump came immediately, right away, by Dr. Kahle, on the sore spot on the back of the neck. . . . I said 'Oh, that was awful.' I said, 'Something terrible has happened to me.' I said, 'That was awful. Let me up. I don't want any more; I can't stand any more.' He said, 'You will be all right. Let me get this other one.' I said 'I have had enough—don't—stop.'" She testified, further, that after she had told the defendant to stop, he continued to give her further adjustment of her neck and up and down the spine. The plaintiff testified that when she went to the defendant's office for treatment she was able to walk, had good eyesight, carried on normal activities, was strong and able-bodied, and suffered only from a stiff neck, headaches and a sore spot behind the right ear. Immediately after the adjustment, the plaintiff was unable to walk, her vision was impaired, she vomited and was in pain, and suffered a partial paralysis of the throat and vocal chords. She was taken from the defendant's office, on a stretcher, to a local hospital and was subsequently removed to the Mayo Clinic at Rochester, Minn., for examination and treatment. According to the testimony of witnesses from the Mayo Clinic, the plaintiff was suffering from a brain tumor when she visited the defendant's office.

It is one of the fundamental duties of a physician, said the Supreme Court, to make a properly skillful and careful diagnosis of the ailment of a patient, and if he fails to bring to that diagnosis the proper degree of skill or care, and makes an incorrect diagnosis, he may be held liable to the patient for the damage thus caused just as readily as he must answer for the application of improper treatment. No good reason exists why the law applicable to physicians, surgeons, dentists, and the like, should not also apply to chiropractors.

Physicians and surgeons who were called by the plaintiff and who were competent to read x-ray pictures of the spine, testified, after examining the x-ray picture of the plaintiff's neck taken by the defendant, that such picture showed no vertebrae out of place. They also testified that other x-ray pictures of the plaintiff's neck taken after she reached the hospital on the day of the adjustment, showed no vertebrae to be out of place. From the evidence in this case, said the Supreme Court, the jury could find the defendant made a wrong diagnosis or analysis of plaintiff's condition, and that her stiff neck, headaches and sore spot behind the right ear were not due to vertebrae out of place; that there were no vertebrae out of place and the x-ray picture, taken by the defendant, so showed; and that defendant should have given plaintiff no adjustment. Continuing, the court said that the jury could also find that during the adjustment, after the plaintiff directed the defendant to stop, the defendant continued adjustment and manipulation with his hands and caused a rupture of a brain tumor, resulting in injury to the plaintiff.

In view of the fact that the jury was warranted in making the above findings, the Supreme Court was of the opinion that the verdict of the jury was not against the weight of the evidence. Accordingly the judgment in favor of the plaintiff was affirmed. *Bakewell v. Kahle*, 232 P. (2d) 127 (Montana 1951).

Admissibility in Evidence of Chemical Tests for Intoxication.—The defendant was convicted of the offense of driving a motor vehicle upon a public highway while intoxicated and appealed to the court of criminal appeals of Texas.

After the defendant's arrest, he was taken to a hospital where a blood specimen was taken from him. At the trial which followed, a chemist for the Department of Public Safety testified that the defendant's blood contained 3.6 mg. of alcohol per cubic centimeter and a physician testified that 1.5 mg. of alcohol per cubic centimeter or more, in the blood would render a person intoxicated. This testimony was admitted in evidence over the defendant's objection that the specimen was taken from him without his voluntary consent and by coercion and persuasion, that the specimen was taken without the warning required under the confession statute having been given and while the defendant was in custody, and that the admission of evidence of the results of the blood test was tantamount to compelling the defendant to give evidence against himself.

The evidence shows, said the court of criminal appeals, that the blood which was taken from the defendant was taken with his consent at the hospital and by a nurse. When a specimen is taken by competent and trained nurses, doctors or laboratory technicians with the consent of one whose sobriety is questioned, the court continued, the results of a blood test thereof may be introduced by the state or by the accused. Consent to the taking of the specimen being shown, the provisions of the fifth amendment to the Constitution of the United States and Art. 1, Sec. 10 of the Constitution of Texas, Vernon's Ann. St. Const., providing that no person shall be compelled to give evidence against himself, are not violated. The purpose of the confession statute referred to by the defendant, said the court, is to prevent the use of verbal statements in the nature of a confession made by an accused while under arrest, and which do not come within the exceptions named in the statute. The provisions requiring that the accused be warned before the confession is made have no application to the obtaining of his consent for blood to be taken for the purpose of analysis.

The defendant's conviction was reversed, however, because there was no showing that the specimen taken by the nurse at the hospital was the same specimen as was examined by the chemist for the Department of Public Safety. *Brown v. State*, 240 S. W. (2d) 310 (Texas 1951).

MEDICAL MOTION PICTURES

Good Eating Habits: 16 mm., black and white or color, sound, showing time 10 minutes. Produced in 1951 by Coronet Instructional Films with the assistance of Clifford J. Barborika, M.D., and James R. Wilson, M.D. Procureable on purchase from Coronet Instructional Films, Coronet Building, Chicago 1.

This is an attitude building film meant to provide reasons for developing good eating habits, which can be understood by children. The story of the film concerns the eating habits of a boy on two succeeding days. On the first day he hurries through breakfast and lunch. He has been given money to buy soup for his lunch, but he spends this for pop and candy after school. Then he is unable to eat the well-prepared dinner his mother has waiting for him, and the results are a stomach-ache and an early bedtime. The next day he eats breakfast leisurely, takes ample time to eat his sandwiches, and uses his lunch money for soup rather than pop and candy. At dinner he is ready and able to eat a good meal. The results of these better habits are that he is not hungry between meals and he feels more like studying and playing hard.

It is not within the purpose of this film to discuss or show food selection and preparation. The facts presented are reasonably accurate but somewhat unrealistic, in that a single attack of indigestion apparently entirely changes the eating habits. The photography and narration are well done. By itself, the film is not completely convincing; however, when used with supplementary teaching materials and elaboration, it is recommended to stimulate discussions in the elementary and junior high grades and also in parent groups.

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Arch. Neurology and Psychiatry, Chicago

66:669-816 (Dec.) 1951

- Subcortical Connections of Temporal Pole in Relation to Temporal Lobe Seizures. C. A. Marsan and J. Stoll Jr.—p. 669.
 Acute Vascular Lesions of Brain Stem: Complication of Supratentorial Space-Occupying Lesions. B. W. Cannon.—p. 687.
 Observations on Effect of Corticotropin in Schizophrenia: Preliminary Report. G. H. Glaser and P. H. Hoch.—p. 697.
 Amnesia—Its Integrative Analysis in Psychopathological Orientation. L. J. Siegel.—p. 700.
 Studies on Excretion of Total Neutral 17-Ketosteroids in Schizophrenic Patients. S. P. Gottfried and I. Minsky.—p. 708.
 *Tetany and Epilepsy. H. Gotta.—p. 714.
 *Papilledema in Poliomyelitis. C. G. Weiman, F. H. McDowell and F. Plum.—p. 722.
 Boeck's Sarcoid with Involvement of Central Nervous System. W. H. Pennell.—p. 728.
 Forced Crying and Laughing: Treatment with Atropine and Atropine-Like Agents. R. Cohn.—p. 738.
 Papilledema in Guillain-Barré Syndrome. A. L. Frew and K. R. Magee.—p. 744.
 Hemiplegia and Thrombosis of Internal Carotid System. A. R. Elvidge and A. Werner.—p. 752.
 Electric Shock Therapy in Case of Myasthenia Gravis Complicated by Schizophrenic Psychosis. R. L. Williams and M. Silbermann.—p. 783.

Tetany and Epilepsy.—Some clinicians regard tetany and epilepsy as completely separate entities that may occur in the same patient, but others assume that tetany is the cause of epilepsy when both conditions are present. The author previously had made electroencephalographic studies on 14 patients with tetany. In this paper he describes six cases of tetany (four postoperative and two idiopathic) in which typical symptoms of epilepsy occurred. He concludes that tetany and epilepsy are separate entities. When they occur together, epilepsy follows tetany. In subjects with an epileptic constitution hypocalcemia precipitates epileptic seizures. Abnormalities in the electroencephalograms of these patients appear in all the leads (frontal, parietal, and occipital); they extend throughout the cortex and are no different from disturbances observed with other types of epilepsy. In all cases of epilepsy of unknown origin, the possibility of parathyroid insufficiency should be considered; symptoms of tetany should be looked for, and the concentration of blood calcium and inorganic phosphate should be determined. In these cases treatment with barbiturates gives no results, but the blood calcium level should be increased by means of calciferol or dihydrotachysterol (Holtz's "A. T. 10"), which gives excellent results if administered long enough in adequate doses.

Papilledema in Poliomyelitis.—Five patients recovering from poliomyelitis accompanied by moderate to severe quadriplegia were found to have papilledema during early convalescence. Papilledema was first observed 11 to 48 days after the acute onset of the illness and persisted from 13 to 140 days, with an average duration of 60 days. It was a benign and self-limited complication. Each patient complained of double vision, and one had associated headache. The visual acuity and visual fields were normal in all five patients. The spinal fluid pressure was elevated in the three patients in whom it was measured. Papilledema in these patients probably represented part of a generalized edema in the central nervous system associated with infection.

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Titles marked with an asterisk (*) are abstracted.

A.M.A. Arch. Surgery, Chicago

63:585-714 (Nov.) 1951

- Experimental Surgical Techniques in Mitral Stenosis. E. Marcus.—p. 586.
 Some Studies on Clotting Activity of Extracts of Normal and Diseased Tissues. A. Blaustein, C. Huber and M. Alberian.—p. 592.
 Increased Intracranial Pressure Following Radical Neck Surgery. R. K. Jones.—p. 599.
 Experimental Artificial Left Heart for Exposure of Mitral Stenosis. A. Kantrowitz, E. Hurwitt and A. Kantrowitz.—p. 604.
 Postcholecystectomy Complications Due to Incomplete Removal of Gallbladder and Cystic Duct: Report of Case of So-Called Reformed Gallbladder. W. B. A. J. Bauer.—p. 612.
 *Endometriosis of Vermiform Appendix: Review of Literature with Addition of Nine New Instances, One of Which Caused Severe Melena. D. C. Collins.—p. 617.
 *Ligation of Hepatic and Splenic Arteries in Patient with Atrophic Cirrhosis of Liver. J. K. Berman, L. P. Muller, C. Fisch and W. Martz.—p. 623.
 Diverticulum of Left Ventricle of Heart: Review of Literature and Report of Successful Removal of Diverticulum. S. Skapinker.—p. 629.
 Internal Biliary Fistula Due to Peptic Ulcer. J. M. Sullivan and L. Hamman.—p. 635.
 Effect of Intraperitoneally Injected Benzalkonium (Zephiran®) Chloride. W. P. Kleitsch and C. F. Heider Jr.—p. 641.
 Cortisone or Corticotropin for Asthmatic Patients Who Require Major Surgical Procedures. L. E. Prickman, G. A. Koelsche, H. M. Carryer and others.—p. 647.
 Tuberculosis Originating from Contaminated Suture Materials and Plastics: Experimental Study. H. J. Corper and M. L. Cohn.—p. 652.
 Thyroiditis. C. P. Schlicke.—p. 656.
 Challenge of the Foreign Body. E. P. Lehman.—p. 663.
 Complications of Intramedullary Fixation of Fractures of Femur. W. G. Stuck and M. S. Thompson.—p. 675.
 *Vagotomy in Treatment of Biliary Dyskinesia. G. Crile Jr. and D. W. Miller.—p. 687.
 Failure of Thymectomy in Lymphatic Leukemia. G. O. Dean, A. M. Earle and W. A. Reilly.—p. 695.

Endometriosis of Vermiform Appendix.—Collins summarizes the data reported in the literature on 134 cases of endometriosis of the vermiform appendix. One case is presented in greater detail because of its unusual clinical features. This apparently is the first recorded instance of severe melena resulting from appendiceal endometriosis. Marked secondary anemia developed within three months following the onset of symptoms. The patient remained well after an appendectomy.

Ligation of Hepatic and Splenic Arteries in Cirrhosis.—Experimental work having shown that ligation of the hepatic and splenic arteries was a rational procedure in the treatment of portal hypertension due to cirrhosis of the liver, it was decided to try the operation on a patient with advanced cirrhosis. He was a man of 60, who for about 30 years had consumed 6 to 10 bottles of beer and 1 to 2 pt. (0.5 liter) of whisky daily. During his first hospitalization in 1949 numerous paracenteses were done, with removal of an average of 17,855 cc. of fluid per month. Then he was treated for five months with a carboxylic type of cation exchange resin in doses ranging from 40 to 90 gm. per day. With this therapy his weight remained relatively constant, only one paracentesis being necessary during this time. Because of anorexia, weakness, and bloody diarrhea, the patient returned to the hospital on April 30, 1950, and the resin therapy was discontinued. Persistent bloody diarrhea associated with a small liver indicated a grave prognosis. During the next six months therapy consisted of a low salt diet and daily injections of mercurial diuretics, but monthly paracenteses were still necessary. On Nov. 21, 1950, the abdomen was opened and approximately 7,500 cc. of straw-colored fluid was aspirated from the abdominal cavity. The liver was small and hard and was covered with a fibrinous exudate. The hepatic artery was doubly ligated and the splenic artery was also ligated, both vessels being tied close to the celiac axis. Up to the time of this report (six months after the ligation), there has been no edema and only slight recurrence of ascites, which receded as soon as a restricted salt diet was instituted. There are indications of increased urinary excretion of sodium. No bleeding has occurred from the esophageal varices or other points in the gastrointestinal tract. The

patient has shown remarkable improvement. Perhaps even better results may be obtained by dividing the arteries instead of simply ligating them, so that recanalization cannot occur. This has been done successfully in five patients recently.

Vagotomy in Biliary Dyskinesia.—Postcholecystectomy colic, or biliary dyskinesia, is a poorly defined syndrome. Some clinicians assume that spasm of the sphincter of Oddi is involved. It may cause symptoms indistinguishable from biliary colic due to a calculus, and the possibility of stone in the stump of the cystic duct, stone in the common duct, and disease of adjoining viscera (duodenal ulcer, recurrent pancreatitis, and renal calculi) must be excluded. Most of the treatments employed are aimed at relaxing spasm of the sphincter of Oddi. Antispasmodics including glyceryl trinitrate may be used, but β -diethylaminoethyl fluorene-9-carboxylate (pavatrine®) hydrochloride or adiphenine (trasentine®) hydrochloride seem most effective. Morphine causes the sphincter to contract and should be avoided. Endocholedochal sphincterotomy, splanchnic nerve section, denervation of choledochus, and removal of a long stump of the cystic duct have been tried as surgical treatment. Since the parasympathetic nervous system through the right vagus nerve has tonic control of the sphincter of Oddi, vagotomy on the right side should relax the spasm. Crile and Miller performed nine vagotomies for biliary dyskinesia. Cholangiograms were made on all but one patient, and the diagnosis of biliary dyskinesia was made by exclusion of organic disease. Five of the nine were subjected to bilateral vagotomy, with good results in three, improvement in one, and failure in one. The remaining four were treated by vagotomy on the right alone, with relief of symptoms in one and slight improvement or failure in three. Patients in whom biliary dyskinesia develops usually are nervous and subject to conversion neuroses. Whenever possible, the symptoms should be controlled by medical or psychiatric therapy.

American Journal of Clinical Pathology, Baltimore

21:999-1100 (Nov.) 1951

- *Blastomycosis. J. Schwarz and G. L. Baum.—p. 999.
- Studies on Platelets: I. Relationship of Platelet Agglutination to Mechanism of Blood Coagulation. M. Stefanini and J. H. Silverberg.—p. 1030.
- Estimation of Lysozyme in Certain Biologic Materials. B. H. Pringle, D. C. DePaulis and T. D. Pemrick.—p. 1039.
- Clinical Evaluation of Middlebrook-Dubos Hemagglutination Test. R. M. Young and W. A. Leonard Jr.—p. 1045.
- Electrocardiographic Changes in Donors During Bloodletting. I. Hoffman, J. Litwins and L. Sussman.—p. 1051.

Blastomycosis.—According to Schwarz and Baum blastomycosis is produced by *Blastomyces dermatitidis*, a biphasic fungus. They present data obtained in 22 cases observed in Cincinnati during the past eight years, and in 36 cases from the files of the Armed Forces Institute of Pathology in Washington. The only absolute diagnostic proof of the disease is obtained by culture. However, demonstration of double-walled, single-budding yeast cells 5 to 20 μ in diameter in exudates or tissues is acceptable proof. Identification of a culture of *Blastomyces* largely depends on the structure and the biphasic character of the growth. The organism should not be confused with *Torula* (*Cryptococcus neoformans*), as has been done in some reports. The capsule formed by *Cryptococcus*, which is absent in *Blastomyces*, is one of the differentiating characteristics. Confusion with *Monilia* and endospores of *Coccidioides immitis* is also possible. Skin tests for blastomycosis, the pathological anatomy of the pulmonary and other forms, the pathogenesis, clinical data, and treatment are discussed. Blastomycosis, a chronic granulomatous disease, is most frequently pulmonary in origin. A tendency to heal is common in the lung and satellite lymph nodes and to some degree in other organs. The disease extends by lymphatic, hematic, or canalicular routes, the hematogenous route being most important. Any organ may be involved. Blastomycetes were repeatedly seen in blood vessels, and once in a blood vessel of an organ (kidney) without blastomycotic granuloma. Blastomycetes were also found in bone marrow. Blastomycotic bronchitis (destruction of bronchial mucosa) in smaller bronchi is a constant finding in cases of active pulmonary disease, and perforation into the parenchyma of the lung has been observed. Cutaneous blastomycosis is most frequently secondary to a primary pulmonary infection. The role of trauma has been over-

emphasized in cutaneous blastomycosis. In pulmonary blastomycosis cavities are uncommon and when present are small necrotic foci without prominent walling-off; pleuritis is always present and is usually dry and fibrinous. Blastomycosis seems to be transmitted by way of the respiratory tract, but the source of infection is unknown. Skin-testing of contacts did not produce evidence for transmission of the disease from man to man. Treatment with iodides is empirical, and antibiotics apparently are of no help. There is little proof that desensitization with vaccine is beneficial. Surgery was of value in four patients with isolated cutaneous lesions.

American J. Digestive Diseases, Fort Wayne, Ind.

18:323-348 (Nov.) 1951

- Influence of Virus Hepatitis on Morphology of Gastric Mucosa. E. D. Palmer.—p. 323.
- Heredity and Diabetes. E. M. Watson and M. W. Thompson.—p. 326.
- Evaluation of Clinical Methods in Gastro-Intestinal Disease: IV. Autopsy Findings of Liver Disease (Fatty Infiltration, Hepatic Cirrhosis) Observed in Peptic Ulcer Cases. A. A. Goldbloom, A. Lieberman and A. Silver.—p. 330.
- Gastric Ulcer: Diagnostic Studies in 100 Cases. J. A. Hagans and M. C. McCord.—p. 335.
- Gallbladder Disease in Men: Need for Earlier Diagnosis and Treatment. S. Hyman and F. Steigmann.—p. 337.
- Use of Multiple Intestinal Adsorbents as Adjunct in Management of Nausea and Vomiting in Pregnancy. V. deP. Fitzpatrick, R. E. Hunter and C. E. Brambel.—p. 340.

American Journal of Ophthalmology, Chicago

34:1483-1648 (Nov.) 1951

- Integrated and Buried Implants. A. P. Drucker, W. W. Kreft, M. D. Pearlman and others.—p. 1483.
- *Effect of Sunglasses in Protecting Retinal Sensitivity. R. H. Peckham and R. D. Harley.—p. 1499.
- Tarsitis as Cause of Sulfonamide Resistance in Trachoma. F. N. Sezer.—p. 1508.
- Tumor of Lacrimal Glands: Report of Four Cases. A. R. Irvine, W. L. Roberts and P. S. Soudakoff.—p. 1511.
- Mixed Tumor of Lacrimal Gland with Extensive Metastases. W. W. McKinney and W. C. Butz.—p. 1519.
- Changes in Corneal Curvature Following Cataract Extraction. G. Floyd.—p. 1525.
- Lint in Anterior Chamber Following Intraocular Surgery. D. Vail.—p. 1533.
- Glaucoma Associated with Polycystic Kidney Disease. W. L. Berkley.—p. 1539.
- Relation of Perceived Size of Half-Images at Fusion Level to Projection on the Horopter: Its Importance in Aniseikonia and Heterophoria. P. W. Miles.—p. 1543.
- Ocular Pemphigus: Report of a Classical Case. P. M. Corboy.—p. 1561.
- Correlation of Surgical Treatment of Essential Hypertension with Blood-Pressure Response Tests and Retinal Changes. S. D. Aiken.—p. 1565.
- Ocular Manifestations of Tropical Diseases. J. M. Varas Samaniego.—p. 1574.
- Etiology of Angular Conjunctivitis. Y. Mitsui, S. Hinokuma and C. Tanaka.—p. 1579.
- Malignant Exophthalmos. M. M. Medine.—p. 1587.
- Clinical Trial of Aureomycin in Trachoma. R. Naccache.—p. 1591.
- Preliminary Report on New Cycloplegic and Mydriatic Drug. R. D. Kiess and F. B. Fralick.—p. 1593.

Sunglasses to Protect Retinal Sensitivity.—The need for visual efficiency during night lookout and sentry duty directed attention to retinal sensitivity. It was learned that exposure to excessive sunlight would seriously decrease night vision, and experiments were undertaken on life guards. They were divided into two groups, depending on whether they stated that they wore sunglasses "always" or "usually," or wore them "seldom" or "never." The following conclusions are drawn from the experimental data: 1. Wearing sunglasses of commercial density (35 to 50%) will protect retinal sensitivity for short periods (one day or less), but not for periods of a week or more. 2. Wearing darker sunglasses will provide protection from exposure to excessive sunlight for as long as a week or more. (Such sunglasses are commercially available, but are in the minority). 3. Failure to wear sunglasses will reduce retinal sensitivity by average of about 50%; in extreme cases the loss can amount to more than 90%. 4. Loss of retinal sensitivity can be assessed as a reduction of the effectiveness of available ambient photopic (cone) illumination. 5. Extravital rays (ultraviolet and infrared) cannot be considered the cause of loss of retinal sensitivity; rather the visible portion of solar radiation is responsible. The

loss of retinal sensitivity after exposure without sunglasses can be a causative factor of industrial and automobile accidents. Night driving after a day at the beach can be dangerous. A small reduction of the effective brightness of fluoroscopic images is a detriment to a radiologist. When fluoroscopy is practiced extensively, use of high density sunglasses is essential. The authors call attention to the difficulty of obtaining sufficiently dark sunglasses. If the wearer's eyes can be seen behind the lenses, the lenses are probably not dark enough.

American Journal of Public Health, New York

41:1333-1454 (Nov.) [Part I] 1951. Partial Index

- Public Health and "Socialized Medicine." W. P. Shepard.—p. 1333.
 Studies of Coxsackie Viruses: Observations on Epidemiological Aspects of Group A Viruses. R. M. Cole, J. A. Bell, E. A. Beeman and R. J. Huebner.—p. 1342.
 Brill's Disease: IV. Study of 26 Cases in Yugoslavia. E. S. Murray, T. Pšorn, P. Djaković and others.—p. 1359.
 Public Health Aspects of Water Fluoridation. H. E. Hilleboe and D. B. Ast.—p. 1370.
 Culture Medium for Detecting and Confirming *Escherichia Coli* in 10 Hours. G. H. Chapman.—p. 1381.
 Public Health Administration in Mental Hygiene. P. V. Lemkau.—p. 1382.
 Biostatistics in Evaluation of Premature Services. F. J. Menchaca.—p. 1388.

41:1-126 (Nov. [Part II]) 1951. Partial Index

- Practical Aspects of Coördinating Maternity Care: Role of Health Departments. J. Whitridge Jr.—p. 5.
 Maternity Service Under Health Insurance Plan of Greater New York. G. Bachr and N. R. Deardorff.—p. 41.
 Objectives and Methods of the New York City Hospital Consultation Program. S. M. Wishik.—p. 68.
 Role of Hospital Consultation Program in Prevention of Prematurity and the Deaths of Prematures. J. B. Faison.—p. 76.
 Obstetric Aspects of the Hospital Consultation Program. E. M. Gold.—p. 80.
 Role of the Pediatrician in the Hospital Consultation Program. H. M. Wallace.—p. 87.
 What and How Shall We Teach Expectant Parents? Point of View of the Pediatrician. M. E. Mercer.—p. 107.

American Journal of Surgery, New York

82:533-670 (Nov.) 1951

- omalous Hypertrophy of Ileocecal Valve. M. Edwards and H. Zangara.—p. 533.
 are Anomaly of Rectum and Lower Urinary Tract. F. J. Burns, L. J. Stephens and H. H. Kramolowsky.—p. 538.
 New Horizons in Proctology: The Third Joseph McDowell Mathews Memorial Oration. F. C. Yeomans.—p. 542.
 Adenoma of Rectum and Lower Portion of Sigmoid: Clinicopathologic Study. W. L. Cooper, L. A. Buie and J. R. McDonald.—p. 546.
 Maximal Diagnostic Potential of Barium Enema in Management of Colon Disease. J. A. Ferguson.—p. 553.
 Amino Acid Therapy for Pruritus Ani. L. G. Bodkin.—p. 557.
 Surgical Management of Idiopathic Pruritus Ani. G. L. Kratzer.—p. 560.
 *Streptomycin in Treatment of Anorectal Tuberculosis: With Particular Reference to Topical Therapy. I. Skir, N. L. Freund and J. M. Gross.—p. 564.
 Prophylactic Oophorectomy with Resection of Large Bowel for Cancer. C. A. V. Burt.—p. 571.
 Total Hysterectomy with Resection of Primary Carcinoma of Bowel: Report of 47 Cases. R. B. Cattell and A. J. Mace.—p. 578.
 Diverticulis and Diverticulitis: General Consideration and Sigmoidoscopic Diagnosis. N. D. Smith.—p. 583.
 Roentgenologic Aspects of Diverticulitis and Its Complications. R. Wigh and P. C. Swenson.—p. 587.
 Intestinovesical Fistula. G. H. Ewell.—p. 597.
 Surgical Aspects of Diverticulitis. N. W. Swinton.—p. 603.
 Benign Lymphoma of Rectum. B. F. Sniderman.—p. 611.
 Proctalgia Fugax. J. D. Karras and G. Angelo.—p. 616.
 Role of Arteries and of Posture in Hemorrhoids. V. C. Tucker.—p. 626.
 Melanosis Coli: Experimental Observations on Its Production and Elimination in 23 Cases. G. S. Speare.—p. 631.
 Consideration of Newer Antibiotics. W. E. Herrell.—p. 638.
 Rectal Complications Following Treatment of Genitourinary Cancer. O. T. Evans.—p. 645.

Topical Use of Streptomycin in Anorectal Tuberculosis.—When Skir and associates began topical application of streptomycin in anorectal tuberculosis in December, 1946, they found few references to the topical use of streptomycin and none to this method in anorectal tuberculosis. Because of its relative stability in solution, rapid action even in the presence of blood, serum, or pus, and relatively low degree of irritation, they decided to try topical application. The histories of 21 patients treated between December, 1946, and November, 1949, are

briefly presented. Streptomycin was first employed as an ointment (33,000 units per gram). In October, 1947, this was abandoned in favor of an emulsion in cod liver oil (2,000 units per cubic centimeter) applied on gauze packing. In November, 1948, the authors changed to a saline solution in the same concentration, which was used for irrigation or to saturate gauze packing. The antibiotic was frequently administered intramuscularly during the latter part of this study as it became more readily available, but always only on the basis of the status of the pulmonary lesion. The authors feel that a statistical evaluation of their results would be meaningless in view of differences in the virulence and sensitivity of various strains, bacterial contaminants, dilution by discharges, and variation in the application. They found, however, that with streptomycin therapy wounds dormant for weeks promptly resumed activity. Burrowing was arrested but fibrosis and vascularization were stimulated, and epithelization and healing generally were accelerated. The intramuscular route seems the most dependable because it allows regular administration and certainty of absorption and systemic effect. The drug is most effective in an aqueous medium. To avoid sensitization, which occurred in three cases, it seems advisable to discontinue local applications after two or three weeks. While topical streptomycin treatment is a valuable adjuvant, surgery remains the basic treatment.

American Review of Tuberculosis, New York

64:477-582 (Nov.) 1951

- *Plastic Reconstruction of Trachea and Bronchi. D. L. Paulson.—p. 477.
 Histologic Study of Blood Vessels in Surgically Resected Tuberculous Lungs. J. Denst, A. Hurst and S. H. Dressler.—p. 480.
 Value of Follow-Up Studies of Children with Primary Tuberculosis. E. M. Lincoln.—p. 499.
 Effect of Adrenocorticotrophic Hormone (ACTH) on Pneumonia Induced with Tuberculin in Lungs of Sensitized Rabbits. O. M. Reinmuth and D. T. Smith.—p. 508.
 Attempts at Passive Transfer of Tuberculin Type of Sensitivity with Living Granulocytes. W. F. Kirchheimer, A. R. Hess and R. G. Spears.—p. 516.
 Relationship Between Virulence of Tubercle Bacilli and Vigor of Their Oxidative Attack upon Certain Substrates. L. H. Geronimus and J. M. Birkeland.—p. 520.
 Relation Between Size of Infecting Dose of Tubercle Bacilli and Survival Time of Mice. G. P. Youmans and A. S. Youmans.—p. 534.
 Assessment of Antituberculous Chemotherapeutic Activity in Mice, Using Virulent Human-Type Tubercle Bacilli. G. P. Youmans and A. S. Youmans.—p. 541.
 Blood Media for Culturing Tubercle Bacilli: Evaluation by Means of Serial Dilution Method. A. W. Frisch and M. S. Tarshis.—p. 551.
 Subcutaneous Administration of Sodium Salt of Para-Aminosalicylic Acid in Treatment of Tuberculosis. B. M. Fisher, G. Roberts and H. C. Hinshaw.—p. 557.

Plastic Reconstruction of Trachea and Bronchi.—Reconstruction of the bronchial or tracheal lumen may be necessary to preserve lung tissue or life itself, since trauma, tumors, tuberculosis, and other infections may obstruct the lumen. Paulson reviews experimental and clinical experiences with reconstruction of the trachea and bronchi and reports three cases in which he used dermal grafts. The first patient sustained a severe chest injury when heavy drill pipe rolled across his chest and neck. Tension pneumothorax and mediastinal emphysema developed, necessitating an emergency mediastinotomy and pleural decompression. The lung expanded well, but seven weeks later progressive atelectasis became evident. Bronchoscopy and bronchography at this time revealed complete occlusion of the right main bronchus at the carina. To save the right lung, a plastic reconstruction of the right main bronchus was accomplished by a dermal graft. Narrowing of the bronchus by scar tissue did not interfere with normal pulmonary function. In the second case, in which the patient had tracheal carcinoma, tracheotomy should have been done at the time of the reconstruction, as frequent intratracheal aspirations did not adequately remove the secretions. In the two days before tracheotomy was done, the lung was irreversibly damaged by obstruction of smaller bronchi. The third patient developed a tracheal stenosis, secondary to a tracheobronchial tuberculosis. Plastic reconstruction of the upper portion of the trachea by dermal graft was successful, but reactivation of submucosal tuberculosis produced bronchial obstruction, resulting in death. Bronchoscopy three weeks following reconstruction of the trachea revealed a satisfactory

mucosal lining. The patient had obtained complete relief from tracheal stridor and exercise tolerance had returned to normal. The author believes wire-enforced dermal grafts are satisfactory for plastic reconstruction of the trachea and bronchi.

Annals of Allergy, Minneapolis

9:703-836 (Nov.-Dec.) 1951

- Pulmonary Distribution of Radioactive Particles in Rabbits After Inhalation and Intravenous Injection. G. V. Taplin, J. S. Grevier, M. L. Gautschi and others.—p. 703.
- Allergy of Urinary Tract: Critical Review of Literature with Analysis of 613 Cases of Urologic Disease in Relation to Allergy. S. C. Dees and E. C. Simmons.—p. 714.
- Phenergan: Clinical Evaluation: Based on Study of 193 Allergic Patients. M. M. Peshkin, H. G. Rapaport and S. Grosberg.—p. 727.
- Studies on Urinary Excretion of 11-Oxycorticosteroids by Allergic Patients Treated with Adrenocorticotrophic Hormone (ACTH). A. J. Stanley, G. S. Bozalis, D. I' Iziff and others.—p. 741.
- Endocrine Hypersensitivity. L. Meltzer.—p. 753.
- Differential Diagnosis of Cough in Tuberculosis and Bronchial Asthma. E. A. Brown.—p. 760.
- New Sympathomimetic Amine ("Neosuprel") in Treatment of Bronchial Asthma. J. A. Herschfus, E. Bresnick, L. Levinson and M. S. Segal.—p. 769.
- Periorbital Dermatitis. B. Swinny.—p. 774.

Annals of Surgery, Philadelphia

134:785-928 (Nov.) 1951

- Development of Surgery for Cancer of Colon. A. W. Allen.—p. 785.
- Benign Extrahepatic Biliary Tract Obstruction: Analysis of 54 Cases. R. D. O'Malley, A. H. Aufses Jr. and A. O. Whipple.—p. 797.
- Experimental Reconstruction of Extrahepatic Biliary System Using Free Venous Grafts. A. E. Pearce, A. W. Ulin, J. H. Entine and G. F. Frolo.—p. 808.
- *Results of Splenectomy: Follow-Up Study of 140 Consecutive Cases. E. M. Miller and A. B. Hagedorn.—p. 815.
- Intertrochanteric Fractures of Hip: Six Year Study of 213 Cases. J. J. Ryan and J. M. Gosslee.—p. 822.
- Neck Dissections in Treatment of Cancers of Head and Neck: Analysis of 221 Patients. T. H. C. Barclay, L. F. Peltier and A. J. Kremen.—p. 828.
- Surgical Significance of Duodenal Diverticula. R. H. Patterson and B. Bromberg.—p. 834.
- Technic and Results of Dependent, Greater Curvature Gastro-Enterostomy. R. S. McCleery, J. E. Kesterson and J. N. Proffitt.—p. 844.
- Acute Pancreatitis, Diagnosis and Treatment. W. E. Sullens and M. E. Lichtenstein.—p. 853.
- Local Recurrence Following Surgery for Cancer of Breast. E. W. Demaree.—p. 863.
- Experimental Studies of Preserved Aortic Homografts. C. C. Coleman Jr., R. A. Deterling Jr. and M. S. Parshley.—p. 868.
- Therapeutic Effect of Aureomycin in Experimental Peritonitis in Dog: II. Parenteral Therapy. F. B. Schweinburg, P. Glotzer, A. M. Rutenburg and J. Fine.—p. 878.
- Metabolic Effects of Paracolon Bacteremia. R. M. Nelson.—p. 885.
- Use of Skin Grafts in Hernia Repair. W. M. Eisele and G. B. Starkloff.—p. 897.
- Total Pancreatectomy for Sarcoma of Pancreas. H. E. Feather and C. L. Kuhn.—p. 904.
- Embolctomy in Acute Mesenteric Occlusion. A. A. Klass.—p. 913.
- Experimental Evaluation in Dog of Esophagogastricomy for High-Lying Gastric Ulcer: Preliminary Report. L. B. Kiriluk and K. A. Merendino.—p. 918.
- Sacculated Aneurysm of Saphenous Vein. K. M. Lippert and L. D. Frederick Jr.—p. 924.

Results of Splenectomy.—Miller and Hagedorn investigated the records and ascertained the present status of 140 consecutive patients who had undergone splenectomy at the Mayo Clinic from 1942 to 1944. Cases in which the spleen was removed as a secondary procedure or for traumatic splenic rupture were not included. Preoperatively 38 of the 140 cases were diagnosed as congenital hemolytic icterus; 47 as essential thrombocytopenic purpura; 45 as Banti's disease or congestive splenomegaly; 5 as acquired hemolytic anemia; and 5 as "indeterminate splenomegaly." The authors feel splenectomy can be performed for any of the conditions associated with hypersplenism with a reasonably low mortality rate. An exception to this statement is congestive splenomegaly, in which the operation has a higher mortality rate than with the blood dyscrasias. In this series of 140 splenectomies there were six deaths, a mortality rate of 4.3%. Success of splenectomy for hypersplenic disorders frequently depends on whether accessory spleens have been found and removed. In the event of recurrence of symptoms, especially in thrombocytopenic purpura, "the uncertainty of finding splenic tissue at (the second) operation makes a surgical procedure prohibitively dangerous." In this series, accessory spleens

were found and extirpated in 25 cases, or 18%. The two hypersplenic conditions for which splenectomy was most valuable were congenital hemolytic icterus and primary thrombocytopenic purpura. In about half of the cases of acquired hemolytic anemia of the primary type, splenectomy produced sustained remissions. Splenectomy is justifiable as a diagnostic measure in the presence of splenomegaly when agnogenic myeloid metaplasia has been excluded by bone marrow studies. Greater emphasis on preoperative bone marrow studies will clarify the indications for, and contraindications to, operative intervention. The discouraging results of splenectomy for congestive splenomegaly should stimulate further investigation for a procedure of curative value.

Cancer Research, Chicago

11:821-898 (Nov.) 1951. Partial Index

- Some Aspects of Nitrogen and Energy Metabolism in Cancerous Subjects: Review. G. B. Mider.—p. 821.
- Liver Nitrogen in Tumor-Bearing Rats. E. H. Yeakel and G. L. Tobias.—p. 830.
- Influence of Pantothenic Acid Deficiency on Viability and Growth of Rat Fibrosarcoma. G. Montañez, E. A. Murphy and M. S. Dunn.—p. 834.
- Subcutaneous Implantation of Whole Mouse Pituitary and Estrous Behavior of Ovariectomized C3H Mice. T. A. Newberry, J. T. King and M. B. Visscher.—p. 851.
- Studies on Ehrlich Ascites Tumor: I. Enzymic and Metabolic Activities of Ascitic Cells and Ascitic Plasma. E. Kun, P. Talalay and H. G. Williams-Ashman.—p. 855.
- Concentration of Folic Acid in Leukocytes: Observations on Normal Subjects and Persons with Leukemia. M. E. Swendseid, F. H. Bethell and O. D. Bird.—p. 864.
- Nitrogen Mustard Inhibition of Azo Dye Carcinogenesis. A. C. Griffin, E. L. Brandt and V. Setter.—p. 868.
- Use of X-Ray and Nitrogen Mustard to Determine Mitotic and Intermitotic Times in Normal and Malignant Rat Tissues. W. R. Widner, J. B. Storer and C. C. Lushbaugh.—p. 877.
- Distribution of Radioactivity in Mice Following Administration of 3,4-Benzpyrene-5-C¹⁴ and 1,2,5,6-Dibenzanthracene-9,10-C¹⁴. C. Heidelberger and S. M. Weiss.—p. 885.

Circulation, New York

4:641-796 (Nov.) 1951

- Heart Disease Case Finding by Means of 70 Millimeter Photofluorographic Films: Group I. D. D. Rutstein, C. R. Williamson and F. E. Moore.—p. 641.
- Id.: Group II. C. R. Williamson, F. E. Moore and D. D. Rutstein.—p. 652.
- *Screening Tests in Mass Surveys and Their Use in Heart Disease Case Finding. D. D. Rutstein.—p. 659.
- Blood Lipids and Human Atherosclerosis: II. Influence of Heparin upon Lipoprotein Metabolism. D. M. Graham, T. P. Lyon, J. W. Gofman and others.—p. 666.
- Effect of Small Doses of Heparin in Increasing Translucence of Plasma During Alimentary Lipemia: Studies in Normal Persons and Patients Having Atherosclerosis. W. J. Block, N. W. Barker and F. D. Mann.—p. 674.
- Distribution of Body Fluids in Congestive Heart Failure: I. Theoretic Considerations. J. R. Elkinton and R. D. Squires.—p. 679.
- Id.: II. Abnormalities in Serum Electrolyte Concentration and in Acid-Base Equilibrium. R. D. Squires, R. B. Singer, G. R. Moffitt Jr. and J. R. Elkinton.—p. 697.
- Regional Vasomotor Tone in Normotensive and Hypertensive Dogs. A. H. Williams and H. A. Schroeder.—p. 706.
- Physiologic and Physical Factors that Govern Clinical Appreciation of Cardiac Thrills. T. B. Counihan, M. B. Rappaport and H. B. Sprague.—p. 716.
- Action of Several Cardiac Glycosides on Conduction Velocity and Ventricular Excitability in Dog Heart. G. K. Moe and R. Méndez.—p. 729.
- Dye Dilution Method for Describing Central Circulation: Analysis of Factors Shaping Time-Concentration Curves. E. V. Newman, M. Merrell, A. Genecin and others.—p. 735.
- Experimental Arterial Disease: I. Reaction of Pulmonary Artery to Minute Emboli of Blood Clot. W. B. Wartman, R. B. Jennings and B. Hudson.—p. 747.
- Id.: II. Reaction of Pulmonary Artery to Emboli of Filter Paper Fibers. W. B. Wartman, B. Hudson and R. B. Jennings.—p. 756.
- Management of Acute Cardiac Emergencies. C. E. de la Chapelle and O. A. Rose.—p. 764.

Screening Tests in Heart Disease Case Finding.—This paper discusses principles of screening tests for case finding in the general population and evaluates heart disease case finding studies carried out in Boston. The making of a 70 mm. photofluorographic film used in the Boston heart disease studies is a standardized procedure that can be performed by average technicians. One unsolved problem is the exposure of the film at a specific phase of the respiratory cycle to avoid fluctuations in heart size

due to changes in intrathoracic pressure during respiration. In order to be valid, a screening test must separate the "true positives" from the "true negatives," and keep to a minimum the number of "false positives" and "false negatives." The majority of those whose films were read as abnormal and who returned for examination had clinically significant heart disease. Thus the number of false positives does not invalidate the practicability of the 70 mm. photofluorographic film as a heart disease case finding procedure. On the other hand, the percentage of false negatives is unknown, because funds for the Boston studies did not provide for follow-up of a sample of those whose films were read as negative. Thus the ratio of false negatives to all negatives could not be calculated. The yield of previously unknown cases discovered and benefited in the Boston surveys was satisfactory, in comparison with yields usually obtained in mass surveys for other diseases. Patient acceptance of the case finding program was evidenced by the return for diagnosis of over three-fourths of those whose films were read as abnormal. However, this high rate of return required concerted follow-up efforts.

Diseases of Chest, Chicago

20:453-574 (Nov.) 1951

- Surgery of Valvular Heart Disease. C. P. Bailey, R. P. Glover and T. J. E. O'Neill.—p. 453.
- Influence of Cortisone on Experimental Tuberculosis of Guinea Pigs. A. G. Karlson and J. H. Gainer.—p. 469.
- Reversible Forms of Heart Disease. J. F. Briggs.—p. 482.
- Oleothorax Following Pulmonary Resection. N. C. Andrews, D. R. Morton, G. M. Curtis and K. P. Klassen.—p. 501.
- *Artificial Pneumoperitoneum in Treatment of Pulmonary Tuberculosis. J. L. Elliott and E. Blair.—p. 520.
- *Treatment of Unusual Pulmonary Amebic Abscess with Chloroquine. A. E. Lindsay, W. H. Gossard and J. S. Chapman.—p. 533.
- Use of Streptomycin in Tuberculosis and Pregnancy: Case Report. A. Froman.—p. 539.
- Tuberculosis in General Hospitals: Need for Control Program. S. Jacobs.—p. 545.
- Tuberculosis Patient in General Hospital. J. S. Edlin, S. Bassin and A. A. Richman.—p. 551.
- Practical Use of Isolation Ward in General Hospital for Treatment of Tuberculosis. R. E. Neff.—p. 557.

Pneumoperitoneum for Pulmonary Tuberculosis.—The literature, mode of action, and method of induction of pneumoperitoneum for pulmonary tuberculosis are reviewed, and 70 cases are analyzed in which this treatment was used. It was found that pneumoperitoneum is a valuable adjunct in the therapy of pulmonary tuberculosis. It can be used alone or with phrenicectomy or phrenic crush. It is a relatively safe procedure, complications being comparatively rare.

Chloroquine for Pulmonary Amebic Abscess.—A case is reported of a man, aged 54, who had been in good health until about four months prior to hospitalization for a prolonged pulmonary infection. During the first three weeks in the hospital he was asymptomatic except for a cough productive of about one oz. (30 cc.) of green purulent sputum daily. Bronchoscopy revealed no evidence of bronchogenic carcinoma, and the bronchial secretions aspirated contained neither tumor cells nor acid-fast bacilli. Subsequently his temperature spiked to 102.4 F, malaise and anorexia became marked, and the liver became larger and tender. The white blood cell count rose, and the sputum became rusty brown. The following day motile trophozoites of *Endameba histolytica* were found in the sputum. Examinations of feces revealed no amebas. Emetine, 1 grain (60 mg.), daily for 10 days, but at the end of this time there was no appreciable change. The sputum remained positive for trophozoites, and the chest roentgenogram was unchanged. Chloroquine was started in doses of 1 gm. daily for two days followed by 0.5 gm. daily for 18 days. Procaine penicillin, 600,000 units daily, was also given to control possible secondary infection. One week after the institution of chloroquine therapy, cough was minimal and the sputum no longer rusty. After 10 days of chloroquine therapy, amebas disappeared from the sputum, and there was demonstrable roentgenographic improvement. It is suggested that the pulmonary amebic abscess resulted from hematogenous spread of amebic parasites from liver to lung. Since emetine alone failed to cause a satisfactory response, and chloroquine induced complete clinical remission, it is felt that chloroquine is a useful agent in pleuropulmonary amebiasis.

Endocrinology, Springfield, Ill.

49:429-564 (Oct.) 1951. Partial Index

- Bioassay of Estrogens Using Mouse Uterine Response. B. L. Rubin, A. S. Dorfman, L. Black and R. I. Dorfman.—p. 429.
- Metabolism of Steroid Hormones, Metabolism of Progesterone and Related Steroids. F. Ungar, R. I. Dorfman, R. M. Stecher and P. J. Vignos Jr.—p. 440.
- Effect of Physiological Amounts of Estrogen on Secretion of Follicle Stimulating and Luteinizing Hormones. W. W. Byrnes and R. K. Meyer.—p. 449.
- Metabolism of Intravenous Testosterone by Experimental Animals. C. D. West.—p. 467.
- Histamine Tolerance in Rats with Intramuscular Adrenocortical Transplants. E. L. Komard and L. C. Wyman.—p. 481.
- "Panendocrinectomy" and Serum Proteins in Dog. R. Baker and G. H. Miller Jr.—p. 484.
- Endocrine Influences on Proteinuria in Rat: Effect of Hypophysectomy. H. C. Goodman, J. Marmorston, A. L. Sellers and others.—p. 490.
- Relation of Adrenal to Blood Formation in Rat. A. S. Gordon, S. J. Pillero and D. Landau.—p. 497.
- Immediate Kidney Response to Acute Stress. ^(OJ) Constantinides.—p. 512.
- Development of Obesity in Force Fed Young Thyroidectomized Rats. R. O. Scow.—p. 522.
- Quantitative Inhibition of Progesterone by Estrogens in Development of Decidua. J. T. Velardo and F. L. Hisaw.—p. 530.
- Response of Thyroid Gland of Rat to Severe Stress. R. Bogoroch and P. Timiras.—p. 548.

Florida Medical Association Journal, Jacksonville

38:307-378 (Nov.) 1951

- Cerebral Arteriography: Its Use in Localization and Diagnosis of Intracranial Lesions. M. M. Greenfield and C. Keedy.—p. 323.
- Treatment of Urinary Frequency in Women. J. C. Hayward, L. M. Orr II and J. B. Glanton.—p. 327.
- Malignant Disease During Pregnancy. H. L. Harrell.—p. 330.
- Fundamentals and Experiences in Use of Refrigerated Homogenous Bone. W. J. Newcomb.—p. 333.
- Some Thoughts for a School Health Program. G. L. Beaumont.—p. 338.

Gastroenterology, Baltimore

19:191-382 (Oct.) 1951

- President's Address: Teaching and Research in Field of Gastroenterology. J. G. Mateer.—p. 191.
- Clinical Evaluation of Caffeine Gastric Analysis in Duodenal Ulcer Patients. J. L. A. Roth.—p. 199.
- *Late Effects on Gastric Acidity of Subtotal Gastrectomy for Gastric and Duodenal Ulcer. A. Cornell and L. Drucker.—p. 216.
- Delayed Excretion of Water with Regular Nocturnal Diuresis in Patients with Nontropical Sprue (Idiopathic Steatorrhea). E. E. Wollaege and B. H. Scribner.—p. 224.
- Eosophageal Sensitivity to Mecholyl in Cardiospasm. P. Kramer and F. J. Ingelfinger.—p. 242.
- Comparison of Effects of Methantheline Bromide (Banthine) and Atropine on Secretory Responses of Vagally Innervated and Vagally Denervated Gastric Pouches. C. F. Code, N. C. Hightower Jr. and G. A. Hallenbeck.—p. 254.
- *Therapeutic Value of Banthine in Gastrointestinal Disorders. F. E. McDonough and P. B. O'Neill.—p. 265.
- Abdominal Masses. IV. Diseases of Genito-Urinary System: Tumors of Kidneys, Carcinoma of Prostate, Ovarian Tumors, Ovarian Cysts, Tubo-Ovarian Abscess, and Uterine Fibromyoma. D. B. Butler and J. A. Barga.—p. 283.
- Abdominal Masses. V. Systemic Diseases and Diseases of Special Regions: Chronic Myelogenous Leukemia, Chronic Lymphatic Leukemia, Lymphosarcoma, Polycythemia Vera, Tumors of Abdominal Wall, and Retroperitoneal Tumors. D. B. Butler and J. A. Barga.—p. 303.
- Bacitracin Therapy in Chronic Bacillary Dysentery. D. N. Silverman.—p. 320.
- Determination of Proteolytic Enzymes and Proenzymes in Human Pancreatic Juice. W. Troll and H. Doubilet.—p. 326.
- Observations on Effect of Orally Administered Atropine on Gastric Response to Insulin in Patients with Duodenal Ulcer. B. F. Gill.—p. 331.
- *Role of Resins in Treatment of Water Retention Associated with Cirrhosis of Liver. R. H. Moser, B. D. Rosenak, R. D. Pickett and C. Fisch.—p. 336.

Subtotal Gastrectomy: Effects on Gastric Acidity.—Subtotal gastrectomy is the preferred treatment for intractable peptic ulcer, because it produces a reduction in acidity or an achlorhydria. Widely differing postoperative acid figures have been reported, because as a rule only single determinations were made just before discharge from the hospital. This investigation was undertaken to determine the late acid values. One or more Reh-fuss test meals were made on 154 patients three or more months after operation. This number included 114 patients with duodenal and 40 with gastric ulcers. In many reported series, gastric

and duodenal ulcer are grouped together. This is incorrect because physiologically these two conditions are different and their therapeutic response to gastrectomy is not the same. In 40 cases of gastric ulcer, postoperative achlorhydria developed in 36 (90%). In four cases in which acid was present, achlorhydria was shown in three with a gruel test meal, but responded to histamine. If gruel alone had been employed, gastrectomy for gastric ulcer would have resulted in achlorhydria in 97% of the cases. Of the 114 patients with duodenal ulcer only 63 (55%) had postoperative achlorhydria. Of the 51 duodenal ulcer patients, who retained free acidity postoperatively, 9 had unsatisfactory results, 4 had jejunal ulcer, and 5 had other complications producing massive gastrointestinal hemorrhage. Reoperation was required in four of these patients.

Methantheline Bromide in Gastrointestinal Disorders.—Methantheline bromide (banthine®), through an anticholinergic action similar to that of atropine, decreases gastric motility, delays gastric emptying, and diminishes peristalsis in the small bowel and colon. McDonough and O'Neil of the Lahey Clinic gave 100 to 400 mg. of methantheline bromide daily in divided doses along with routine treatment to 170 patients with peptic ulcer or other gastrointestinal disorders characterized by hypermotility or hypersecretion, or both. As a result, four patients with acute duodenal ulcer were promptly benefited, and their ulcer healed. Fifty-nine of 100 patients with chronic recurrent duodenal ulcer were symptomatically relieved and did not have a recurrence when one could be expected according to their previous history. An additional 10% of the patients, although they had a recurrence, are continuing methantheline therapy, because it lessened either the frequency or severity of their recurrences. All three patients with jejunal ulcer were relieved and their ulcer healed. Two of four patients with gastric ulcer failed to respond favorably. Three of six patients with hyperchlorhydria, three of five patients with hypertrophic gastric rugae, and three of four patients with hiatus hernia were not benefited. Seven of 10 patients with resection of from 7 to 300 cm. of ileum and of the right colon, with ileotransverse colostomy, were symptomatically improved. One patient with a hyperfunctioning ileostomy was benefited, the other was not. Only 10 of 17 patients with the irritable colon syndrome were benefited. Two patients with the dumping syndrome were relieved. None of three patients with chronic relapsing pancreatitis was relieved of pain. Approximately 11% of the 170 patients were unable to continue taking methantheline because of undesirable reactions. The authors regard methantheline as a valuable addition to existing therapeutic methods for duodenal ulcer, but it does not supplant conventional therapy, and it will not always prevent complications, nor intractability. In disorders characterized by intestinal hypermotility, methantheline relieves symptoms if the hypermotility is not secondary to partial obstruction.

Resins for Water Retention in Cirrhosis of Liver.—Sodium retention is apparently an important factor in ascites and/or edema associated with cirrhosis of the liver, but restriction of sodium involves reduction of protein intake to a level that is incompatible with modern concepts of the therapy of liver disease. If it were possible to allow the patient to partake of a diet only moderately restricted in sodium and at the same time prevent absorption of sodium from the gastrointestinal tract, then the two principles of liver therapy would not be compromised. The sodium-removing resins may provide the answer to this problem. Consequently, Moser and associates investigated the effect of such resins in eight patients with cirrhosis, whose ascites did not respond to salt restriction and supplemental salt-poor protein in the diet. A mixture of resins was used containing 59% of a carboxylic acid type of cation exchanger in the hydrogen cycle, 29% of the potassium salt, and 12% of a weakly basic polyamine formaldehyde anion exchanger resin. In five of the patients the ascites was controlled by simultaneous administration of 30 to 50 gm. of resins and restriction of the sodium intake to 1.5 gm. per day. In the sixth patient a lowering of the plasma carbon dioxide content necessitated a reduction in the dose of resin to 40 gm. per day and in the salt intake to 1 gm. per day. Ascites was controlled in the hospital but recurred at home, presumably due to failure to restrict sodium intake

properly. In the seventh patient control was possible with 50 gm. of resin and 3 gm. of sodium daily. The eighth patient was treated for only eight days, during which time the weight remained stationary. Significant sodium and potassium depletion occurred in one case, and potassium depletion in another. Symptoms of hypokalemia disappeared following administration of potassium salts. The authors feel that resins are an important tool for control of water and salt retention due to cirrhosis of the liver. However, this form of therapy is not without some hazard, in that acidosis or at least a diminution of the plasma content of carbon dioxide may occur.

Georgia Medical Association Journal, Atlanta

40:444-500 (Nov.) 1951

- Clinical Approach to Congenital Heart Disease. J. W. Hurst.—p. 451.
- Rectal Bleeding. L. J. Rabhan.—p. 464.
- *Cat-Scratch Disease. I. L. Bennett Jr. and J. T. Melton.—p. 466.
- Coccidioidomycosis: Report of Case in Georgia. F. H. Stubbs and J. L. Dixon.—p. 469.
- Freedom from Government. E. Hess.—p. 474.
- Possible Atomic Bomb Effects Applied to Atlanta. C. E. Dowman.—p. 476.
- Medical Aid Plan for Civil Defense Metropolitan Atlanta Area. C. Eberhart.—p. 481.

Cat-Scratch Disease.—A benign suppurative lymphadenitis occurring after cat scratches was described by French observers in 1950 and subsequently other reports appeared in the European and American literature. However, Foshay, who studied several (unreported) cases in Cincinnati in 1932, is credited with having first called this entity "cat-scratch fever." Bennett and Melton present histories of five patients with cat-scratch disease recently observed in Atlanta. This subacute suppurative lymphadenitis often, though not invariably, follows exposure to cats. Its occurrence following exposure to other animals, including birds, has been described, and there have been cases in which the pathogenic agent was apparently introduced by other minor traumata such as scratches by thorns. Local manifestations are adenopathy, bubo formation, and draining sinuses; the systemic manifestations are usually slight and transient. The disease is probably due to a virus, although no specific agent has been isolated. Pathologically the lesion consists of a granulomatous lymphadenitis with abscess formation. The diagnosis is established by skin testing with antigen prepared from aspirated pus. The course is benign but may be prolonged. Aureomycin and terramycin may be effective in therapy.

Illinois Medical Journal, Chicago

100:273-324 (Nov.) 1951

- Diagnosis and Treatment of Meningitis. A. L. Hoyne.—p. 285.
- Acute Appendicitis. P. Thorck.—p. 290.
- Obstetric Helps. C. O. McCormick.—p. 297.
- Evaluation of Five Years Experience with Continuous Caudal Anesthesia. C. Greenstein.—p. 305.
- Radioactive Digitoxin. F. E. Kelsey.—p. 309.
- Galactose Tolerance Test. A. Kraft and W. Wolf.—p. 311.
- Bleeding from Unsupervised Use of Dicumarol. H. J. Levine and H. E. Ryan.—p. 314.

Journal of Bacteriology, Baltimore

62:519-676 (Nov.) 1951. Partial Index

- Nonadaptive Nature of Change to Full Streptomycin Resistance in *Escherichia Coli*. H. B. Newcombe and J. McGregor.—p. 539.
- *Chemically Defined Medium Suitable for Production of High Titer Diphtherial Toxin. R. M. Drew and J. H. Mueller.—p. 549.
- Studies of Sulfur Metabolism of *Brucella Suis*. L. J. Rode, C. E. Lankford and V. T. Schuhardt.—p. 571.
- Nutrition of Heterofermentative Lactobacilli that Cause Greening of Cured Meat Products. J. B. Evans and C. F. Niven Jr.—p. 599.
- Allergic Property of Scarlatinal Toxin. D. A. Boroff.—p. 627.
- Further Observations on Zone Phenomenon in Bactericidal Action of Penicillin. H. Eagle.—p. 663.

Medium for Production of High Titer Diphtherial Toxin.—The amino acid requirements of *Corynebacterium diphtheriae*, Toronto strain of Park-Williams no. 8, were investigated. It was shown that excellent growth and toxin production can be obtained on a medium composed of eight amino acids, ammonium sulfate, trace metals, inorganic salts, four accessory growth fac-

tors, and maltose. The amino acids include glutamic acid, cystine, proline, tryptophan, leucine, valine, methionine, and glycine. Ammonia could be utilized as a partial source of nitrogen. Thiamine is an additional growth stimulatory factor for the Toronto strain because of its accelerating effect on the rate of growth and toxin-formation. The proposed medium compares favorably with casein hydrolysate medium in its capacity to support the production of high titer diphtherial toxin.

Journal of Immunology, Baltimore

67:379-448 (Nov.) 1951

- High Intensity Electrons as Tool for Preparation of Vaccines: I. Preparation of Rabies Vaccine. F. B. Traub, U. Friedemann, A. Brasch and W. Huber.—p. 379.
- Pig Complement and Its Fractionation for Production of Reagents Containing Third Component. J. Jonsen, W. Manski and M. Heidelberger.—p. 385.
- In Vivo Stability of I^{131} Protein Label of Rabbit Antibody in Guinea Pigs as Determined by Quantitative Precipitin Reaction. L. R. Melcher and S. P. Masouredis.—p. 393.
- Studies on Vaccinia Virus: I. Development of Hemagglutinating and Infective Particles in Chorioallantois of Chick Embryo. B. A. Briody and C. Stannard.—p. 403.
- Id.: Neutralization of Vaccinia Virus by Normal Guinea Pig Serum. B. A. Briody, N. Ledinko and C. Stannard.—p. 413.
- Effect of Proflavine on Growth of Viruses in Chick Embryo. B. A. Briody and C. Stannard.—p. 423.
- Mouse-Egg Neutralization: Neutralization in Mouse of Influenza Viruses Not Adapted to Mouse. E. D. Kilbourne and F. L. Horsfall Jr.—p. 431.
- Comparison by Means of Complement-Fixation Test of Relative Potencies of Chloramphenicol, Aureomycin, and Terramycin in Experimental Q Fever Infections in Embryonated Eggs. R. A. Ormsbee and E. G. Pickens.—p. 437.

Journal-Lancet, Minneapolis

71:473-514 (Nov.) 1951

- Cortisone in Allergic Asthma. J. S. Blumenthal.—p. 473.
- ACTH and Cortisone in Ophthalmology. J. P. Wendland.—p. 482.
- Fatigue States Associated with Abnormal Carbohydrate Metabolism. G. A. Cronk.—p. 484.
- Early Diagnosis of Malignant Lesions of Genito-Urinary System. B. C. Corbus Jr.—p. 488.
- Difficulty in Removing T-Tubes from Bile Ducts. A. L. Cameron.—p. 491.
- Problems in Management of Severe Diabetes. H. O. Mosenthal.—p. 493.
- Index Tract in Medical Literature. J. A. Bargen.—p. 497.

Journal of Pediatrics, St. Louis

39:519-644 (Nov.) 1951

- *Transmission of Poliomyelitis Virus: Analysis of Differing Interpretations and Concepts: Practical Implications. A. B. Sabin.—p. 519.
- Various Aspects of Adolescence. J. R. Gallagher.—p. 532.
- Aureomycin Treatment of Diphtheria and Diphtheria Carriers. S. Karelitz, H. King and I. S. Rubinstein.—p. 544.
- *Treatment of Pertussis with Aureomycin, Chloramphenicol, and Terramycin. L. Weinstein, R. Seltzer and C. T. Marrow III.—p. 549.
- Citrovorum Factor in Leucemia: Two Cases with Autopsy Findings. A. M. Earle, W. A. Reilly and W. G. Lawson.—p. 560.
- Nummular Eczema in Children: Report of Six Cases. H. H. Perlman, J. Gropen and P. Westfall.—p. 565.
- Congenital Atresia of Bile Ducts Associated with Erythroblastosis Fetalis. J. T. McGeehan, J. B. Butchart and D. P. Walker.—p. 575.
- Growth and Development of Infants Receiving Proprietary Preparation of Evaporated Milk with Dextri-Maltose and Vitamin D. L. H. Frost and R. L. Jackson.—p. 585.
- Electrocardiographic Changes in Exchange Transfusions. J. E. Gustafson.—p. 593.
- Hypothyroidism Following Thyroidectomy for Congenital Obstructive Goiter. N. Schiffrin and E. S. Hurwitt.—p. 597.
- Method Adapted for Determination of Urinary 17-Ketosteroids in Children: With Some Considerations of Interpretation. A. M. Bongiovanni.—p. 606.

Transmission of Poliomyelitis Virus.—The virus of poliomyelitis in man is found in the central nervous system and in the digestive tract. Tests of the infectivity of saliva and mouth spray have yielded negative results. Studies have indicated that pharyngeal secretions are neither a source of virus-laden droplets for arial transmission of the infection nor a significant source of virus for contamination of the hands. Thus, there is no evidence that the virus is transmitted by the respiratory organs. Moreover, this hypothesis implies transmission by casual association with exposure to virus-laden droplets rather than by the intimate association that appears to be most important in

transmission of poliomyelitis. The virus occurs in feces of patients and of healthy carriers. It has been detected in stools with a frequency of 70 to 90% during the first week of illness and about 50% during the third and fourth weeks. The virus may be transmitted by feces in intimate association and other ways. The commonest mode of infection is through the mouth; contaminated food and drinks are as important as contaminated fingers. The period of communicability cannot be limited to a few days after onset; it should be regarded as potential as long as the virus is present in the feces. The role of filth flies as transmission agents of stool-borne virus may be important under different circumstances and conditions. More virulent strains may be in circulation in a community during an epidemic period. Measures to combat filth flies and minimize contamination of food should be taken, and elementary rules of hygiene aiming to diminish the individual's chances of infection should be observed.

Aureomycin, Chloramphenicol, and Terramycin in Pertussis.—Antibiotics were given to 80 children with pertussis, without complications at time of admission. Aureomycin was given to 19 patients, of whom 13 were less than one year old; chloramphenicol was given to 36, of whom 16 were less than one year old; and terramycin was given to 25, of whom 14 were less than one year old. The drugs were administered orally in divided doses of 50 to 70 mg. per kilogram of body weight daily for 14 days. In very young children the drugs were given rectally in daily doses of 100 mg. per kilogram of body weight. Three injections of 20 cc. of human hyperimmune serum were given every 48 hours to 35 children less than one year of age. Results showed that aureomycin, chloramphenicol, and terramycin had little or no effect in reducing the incidence or severity of coughing in the paroxysmal phase of pertussis. Terramycin was the most efficient of the three drugs in eliminating H. pertussis from the respiratory tract. Flora changes in the nasopharynx revealed the presence of some potentially pathogenic organisms that were not detected in the culture taken before the therapy and that became numerically significant after treatment was instituted. The number of complications due to secondary bacterial infections (bronchopneumonia, suppurative otitis, and monilial stomatitis) was lowest in patients treated with terramycin. In the aureomycin-treated children the incidence was greater than in untreated patients. Many of these infections were caused by bacteria that rarely induce complications in untreated cases. Terramycin is most effective in decreasing risks of complications and is the drug of choice when prophylaxis of secondary infection is attempted. The best treatment for pertussis is good nursing care, maintenance of adequate nutrition, hydration and electrolyte balance, and early and intensive treatment of complications.

J. Pharmacology & Exper. Therap., Baltimore

103:215-336 (Nov.) 1951. Partial Index

- Toxicity Studies on Amberlite XE-96, Carboxylic Type Cation Exchange Resin. T. L. Flanagan, M. F. Sax and A. E. Heming.—p. 215.
- Further Studies on (RC) Analogue of Acetylcholine and Some Additional Derivatives. F. W. Schueler and H. H. Keasling.—p. 222.
- Comparative Actions of Analgesic, Hypnotic and Paralytic Agents on Hindlimb Reflexes in Chronic Spinal Dogs. R. W. Houde, A. Wikler and S. Irwin.—p. 243.
- Some Actions of Procaine and Related Compounds on Dog's Auricle and A-V Connections. B. B. Brown and G. H. Acheson.—p. 269.
- Effects of Synthetic Curare-Like Compound, Tri-Iodo Salt of Tris (Triethylaminoethoxy) 1, 2, 3 Benzene (Flaxedil), on Anesthetized Surgical Patient. B. E. Marbury, J. F. Artusio Jr., W. C. Wescoe and W. F. Riker Jr.—p. 280.
- Comparative Pharmacology of Isomeric Nitrogen Methyl Substituted Heptylamines. D. F. Marsh, A. Howard and D. A. Herring.—p. 325.
- Pharmacology of 1,1-Dimethyl-4-Phenylpiperazinium Iodide, Ganglion Stimulating Agent. G. Chen, R. Portman and A. Wickel.—p. 330.

Kansas Medical Society Journal, Topeka

52:473-524 (Oct.) 1951

- Cerebrovascular Accident: Review of Some Pathological and Clinical Problems. A. T. Steegmann.—p. 473.
- Cardiac Arrest with Successful Resuscitation. J. Tiller.—p. 480.
- Diverticulitis of Sigmoid as Surgical Problem. E. S. Brinton.—p. 482.
- Psychosomatic Problems of Involutional Period. A. J. Enelow.—p. 486.

Michigan State Medical Society Journal, Lansing

50:1193-1304 (Nov.) 1951

- Calcinosis: Report of Case with Treatment. H. A. Freund.—p. 1233.
 Clinical Evaluation of Polythionates in Dermatology. J. R. Delaney and J. J. Mahood.—p. 1236.
 Restoration of Conceptive Ability Following Surgical Sterilization. C. A. Paukstis.—p. 1238.
 Accident Prevention Through Epidemiologic Analysis. J. E. Gordon.—p. 1239.
 Diagnosis and Treatment of Congenital Urethral Valves. R. M. Nesbit, R. L. Thirlby and F. P. Raper.—p. 1244.
 Silicosis Encountered Among Automobile Workers. I. D. Fagin and H. Balberor.—p. 1248.
 Tuberculosis Control Program in Mental Institution. J. L. Isbister, P. C. Robertson, L. Stanley and C. J. Stringer.—p. 1251.
 Narcoanalysis with Surital Sodium. E. O. Brown Jr.—p. 1255.
 Diagnosis and Treatment of Chronic Diseases of Small Intestine. E. D. Kiefer.—p. 1258.

New England Journal of Medicine, Boston

245:671-710 (Nov. 1) 1951

- "Two Centuries of Service—What of Next?" D. A. Clark.—p. 671.
 Psychiatric Aspects of Cerebral Arteriosclerosis. E. B. Allen.—p. 677.
 *Carcinoma of Cervix: Survival in 98 Cases Treated with Five-Day Radium Only. J. W. Bell, J. V. Meigs and C. H. Swan.—p. 684.
 Mediterranean Anemia (Hereditary Leptocytosis) in a Chinese Family. J. H. Silverberg and D. Shotton.—p. 688.
 Dental Decay and Its Control. P. K. Losch.—p. 690.

Carcinoma of Cervix Treated with Radium Only.—The records of 98 women who had received 6,000 milligram hours or more of radium for carcinoma of the cervix were carefully reviewed. Platinum needles containing 1, 2, and 3 mg. of radium were inserted circumferentially, the 3 mg. needle usually in the center of the growth and the 1 and 2 mg. needles on the periphery. The needles usually remained five days in situ, in some cases four days. A second dose of radium was used only for palliation or local recurrence. Three fourths of the patients had lesions described as either Stage 2 or 3. The radium treatment was designed chiefly for Stage 1 and 2 growths. It was realized that radium might be only a palliative measure in the treatment of Stage 3 and 4 neoplasms. The table listing the five-year survival rates indicates that of the 19 in Stage 1, 12 survived for five years or longer; of the 36 in Stage 2, 18 survived; of the 38 in Stage 3, 17 survived; and of the 5 in Stage 4, none survived. Thus of a total of 98 women with cervical cancer 47 survived more than five years. After 10 years 15 of the women were alive and well. Many observers feel that the average dose of 7,200 milligram hours is too large for women with Stage 1 and 2 lesions, causing unnecessary complications. Severe pelvic radiation reaction occurred in five patients, leading to development of a recto-vaginal fistula in four patients and to vesicovaginal fistula in one. Pyometrium occurred in one patient and pelvic or retroperitoneal hematomas in three. Two patients died of radiation ileitis with perforation and peritonitis. Intestinal obstruction necessitated laparotomy in two patients. At follow-up examinations 17 patients had considerable postirradiation fibrosis and thickening in the broad ligament. Delayed radiation reaction (after three and five years) occurred in two patients. Postirradiation complications of the urinary tract numbered 18 in all and included hydro-nephrosis, ureteral obstruction, radiation cystitis, incontinence, pyelonephritis, and uremia.

New Jersey Medical Society Journal, Trenton

48:493-536 (Nov.) 1951

- Oil Embolism Complicating Hysterosalpingography. N. Karshmer and W. Stein.—p. 496.
 Primary Splenic Neutropenia. S. Friedenberg and R. S. Cotton Jr.—p. 499.
 Diagnosis of Cancer of Esophagus and Stomach. J. E. Berk.—p. 501.
 X-Ray Department in Civilian Catastrophes. E. F. Klein and B. Copleman.—p. 505.
 Eosinopenia in Status Asthmaticus: Report of Two Cases. P. B. Jennings.—p. 507.
 Trime-ton Maleate in Allergic Eye Manifestations. E. Kahan and G. Z. Carter.—p. 510.
 Avitaminosis and Respiratory Moniliasis. R. A. Hall.—p. 512.
 Epiphrenic Esophageal Diverticulum: With Report of Case. F. A. Marshall.—p. 513.
 Treatment of Acute Subacromial Bursitis. H. Merliiss.—p. 515.
 Treatment of Trichinosis with Cortisone. F. Rothenberg.—p. 517.

New York State Journal of Medicine, New York

51:2439-2550 (Nov. 1) 1951

- Clinical Value of Uterosalpingography. H. G. LaForge.—p. 2475.
 Inversion of Puerperal Uterus. D. C. McGill and E. R. Duggan.—p. 2481.
 Myomas in Pregnancy. R. J. Lowrie and K. Rosenberg.—p. 2485.
 Value of Endometrial Curettage in Diagnosis and Treatment of Functional Uterine Bleeding. E. S. Taylor and J. C. Lombardi.—p. 2488.
 Ectopic Pregnancy as Cause of Maternal Mortality in Brooklyn. A. H. Rosenthal and M. Glass.—p. 2493.
 Anesthesia in Cesarean Section. H. S. Acken Jr., R. Waelsch and J. H. Ray III.—p. 2499.
 *Cortisone in Allergic Purpura of Children. I. N. Kugelmass.—p. 2504.
 Mesothelioma of Peritoneum. J. Rosenthal and M. Connor.—p. 2507.
 Toxic Hepatitis Caused by Prolonged Inorganic Arsenic Intake: Studies on Liver Dysfunction—VII. L. Plener and S. Waldman.—p. 2511.
 Nonpenetrating Injuries of Chest. W. W. Heroy and F. C. Eggleston.—p. 2515.
 Acceleration of Blood Transfusions with Intravenous Procaine. N. Neustrup and J. Milowsky.—p. 2520.
 Diagnostic Value of Liver Punch Biopsy. W. Aronson, J. C. Di Lorenzo and E. Katz.—p. 2523.

Cortisone in Allergic Purpura.—Allergic purpura with or without thrombocytopenia is usually accompanied by other allergic manifestations such as urticaria, angioneurotic edema, asthma, lymphadenopathy, arthritis, fever, and leukocytosis. When allergens are numerous and damage to the capillary endothelium widespread, repair of vascular injury may require weeks or months. With cortisone purpuric bleeding can be arrested in hours or days instead of weeks or months whether or not the offending allergens are eliminated. The author presents the histories of four children with allergic purpura who responded to treatment with cortisone. Two children with thrombocytopenia responded promptly to cortisone following a rapid increase of blood platelets and return to normal levels within a week. In the Henoch type of allergic purpura gastrointestinal disturbances cleared within 36 hours, purpuric manifestations within 48 hours, capillary fragility within 72 hours, and blood in urine and stools in 84 hours. In the Schönlein type of allergic purpura appetite improved promptly, fever dropped in 24 hours, joint pains disappeared in 48 hours, purpura faded in 96 hours, and the sedimentation rate was normal in five days. Mild manifestations of allergic purpura remained for weeks after the withdrawal of cortisone.

Northwest Medicine, Seattle

50:825-908 (Nov.) 1951

- *Poliomyelitis in Adults in Seattle in 1949. J. L. Bakke and J. W. Haviland.—p. 846.
 Effect of Pregnancy on Mortality Rate of Tuberculous Woman. N. P. Murphy.—p. 851.
 Pleomorphic Adenoma and Adenocarcinoma of Parotid Gland. W. J. Sinclair.—p. 852.

Poliomyelitis in Adults.—Sixty cases of poliomyelitis in adults observed in one hospital in Seattle during one season are reviewed, and it is assumed that they are representative of the cases observed over the entire state. Three of the 60 patients died of poliomyelitis, a mortality of 5%, which is consistent with the mortality of 5.9% reported for 235 patients over 13 years of age in the entire state during this period. All three deaths occurred in men with bulbar involvement. There were 32 men and 28 women. Of the men, 27 had paralysis, but only 15 of the women had paralysis; 16 of the 23 patients with bulbar involvement were men. Comparing these figures with those for the entire state, it was found that the age and sex distribution of the cases reviewed here was normal. It is the general consensus that the incidence of poliomyelitis in pregnant women is greater than in the general population, and that they are more susceptible to bulbar paralysis. In this series there were 11 female patients over 15 years of age with the paralytic type of poliomyelitis. Three of these were pregnant at three, six, and seven months, respectively, and all three had bulbar paralysis. History of a prodrome is much less frequent among adults than among children. The electrocardiograms of 3 of 13 patients showed abnormal function. Attempts to isolate poliomyelitis virus from fresh myocardium of a fatal case with clinical evidence of myocarditis were unsuccessful. Tracheotomy is an important adjunct in treatment of bulbar cases, but it should not be done routinely. Predominance of palsy in dominant limbs was noted and is offered as evidence for the fatigue theory of paralytic involvement.

Radiology, Syracuse, N. Y.

57:477-628 (Oct.) 1951

- Dural Sinus Venography. B. S. Ray, H. S. Dunbar and C. T. Dotter.—p. 477.
- Cerebral Arteriography in General Hospital Practice. R. C. Moore.—p. 487.
- *Diagnosis of Complete Transposition of Great Vessels. H. L. Abrams, H. S. Kaplan and A. Purdy.—p. 500.
- *Asymptomatic Gastric Mucosal Prolapse. E. J. Levin and B. Felson.—p. 514.
- Rupture of Spleen: Roentgen Diagnosis. J. Gershon-Cohen, M. B. Hermel, R. N. Byrne and L. S. Bringham.—p. 521.
- Combined Radiation Therapy and Surgical Treatment of Technically Inoperable Cancer. G. T. Pack and T. R. Miller.—p. 529.
- Use of ACTH and Cortisone in Treatment of Post-Irradiation Pulmonary Reaction. S. W. Cosgriff and M. M. Kilgerman.—p. 536.
- Olfactory Esthesioneuro-Epitheliomas. W. B. Seaman.—p. 541.
- Chondroangiopathia Calcarea seu Punctata: Review and Case Report. E. R. Haynes and W. F. Wangner.—p. 547.
- Clinical and Roentgen Observations of Newly Perforated Peptic Ulcer. A. J. Winham and G. R. Pechstein.—p. 551.
- Fictitious Pelvic Mass. S. L. Beranbaum.—p. 554.
- The Johns Hopkins Fluoroscopic Screen Intensifier. R. H. Morgan and R. E. Sturm.—p. 556.
- Effect of Single Massive Doses of Roentgen Radiation upon Liver: Experimental Study. I. M. Aric.—p. 561.

Diagnosis of Complete Transposition of Great Vessels.—This is a report of 10 cases of transposition of the great vessels, 9 proved by autopsy and 1 by angiocardiology. The data on these cases were compared with those of 150 cases collected from the literature. The aim was to amplify and clarify the criteria for diagnosis. Transposition of the great vessels is much more frequent in males than in females and few of the children reach the age of 5 years. An enlarged right ventricle was one of the common denominators of most of the reported cases for which adequate autopsy data were available. In some patients the right auricle was enlarged, and the left ventricle was frequently enlarged. Associated shunts, such as patent ductus arteriosus, patent foramen ovale, interauricular septal defect, or interventricular septal defect, were nearly always present. The most frequent clinical findings in the reported cases were early severe cyanosis, with associated dyspnea, clubbing, and polycythemia; cardiac enlargement; variable murmurs, usually systolic; and right axis deviation. Studies on their own cases convinced the authors that the cyanosis is usually uniform in distribution; murmurs and their intensity and transmission depend on the shunts and the state of compensation; and arm and leg pulses are usually normal. The most important roentgenologic signs of transposition of the great vessels are increased heart size, a cephalolateral bulge in the left midcardiac border, a narrow mediastinal shadow in the frontal projection, widening of the great vessel shadow in the left anterior oblique projection, prominence of the pulmonary arterial branches, and right and left ventricular enlargement. Both the clinical and the roentgenologic aspects of the transposition of the great vessels must be taken into consideration in differentiation from tricuspid atresia, the tetralogy of Fallot, the Eisenmenger complex, and the Taussig-Bing syndrome. The cardiac configuration in complete transposition of the great vessels is not pathognomonic. A similar appearance may be seen in cases of coarctation of the aorta of the infantile type, interventricular septal defect, and various types of acquired heart disease. The diagnostic value of the roentgenographic appearance of the heart lies in the fact that it is usually distinctly different from the appearance in the other common cyanotic congenital cardiac malformations.

Asymptomatic Gastric Prolapse.—Unquestionably, patients with prolapse of the gastric mucosa often have symptoms that have been relieved by various therapeutic measures, including diet, antacids, psychotherapy, and surgery. It has never been established, however, that the prolapse is actually the cause of these symptoms and not simply an incidental finding. The fact that Levin and Felson occasionally observed significant degrees of prolapse unassociated with gastrointestinal complaints increased their uncertainty and led them to determine the incidence in asymptomatic patients. They made roentgenologic studies on the upper gastrointestinal tract of 100 patients who had no gastrointestinal symptoms and observed prolapse of the gastric mucosa in 18 cases. The prolapse was slight in 10, moderate in 5 and severe in 3 of the patients. The authors feel that the clinical significance of gastric prolapse has been overemphasized, and that it is seldom the cause of symptoms.

Southern Medical Journal, Birmingham, Ala.

44:993-1088 (Nov.) 1951

- *Hypercholesterolemia. A. McMahon, H. N. Allen, C. J. Weber and W. C. Missey Jr.—p. 993.
- Supernumerary Ureter, Blind at Cephalic End, with Ectopic Opening into Anterior Urethra: Case Report. W. A. Farmer and J. Mendeloff.—p. 1002.
- Volvulus of Colon. L. Rademaker and E. L. Royer.—p. 1005.
- Medical Treatment of Peptic Ulcer. A. Weinstein.—p. 1008.
- Surgical Treatment of Peptic Ulcer. R. M. Larsen.—p. 1016.
- Clinical Features of Walled Off Perforated Peptic Ulcer: Analysis of 100 Cases. C. Cassel, J. M. Ruffin and F. C. Bone.—p. 1021.
- Problem of Silent Gallstone. R. M. Moore, A. F. Kauffmann III and J. P. McNeill.—p. 1027.
- Appraisal of ACTH and Cortisone as Therapeutic Agents. T. D. Spies, R. E. Stone, G. Garcia-Lopez and others.—p. 1034.
- *Simple or Radical Mastectomy: Analysis of Case. W. R. Deaton Jr. and H. H. Bradshaw.—p. 1042.
- Management of Borderline Pelvis. W. E. Brown.—p. 1046.
- Sterility. W. F. Mengert.—p. 1050.
- Psychic Aspects of Sterility and Abortion. T. E. Mandy, E. Scher, R. Farkas and A. J. Mandy.—p. 1054.
- Evaluation of Treatment of Thyroiditis. J. H. St. John and W. M. Nicholson.—p. 1059.
- Conservative Management of Painful Shoulder. D. L. Rose.—p. 1063.
- Thermal Allergy: Clinical Evaluation and Management. H. J. Rinkel.—p. 1067.
- Xylocaine®: New Local Anesthetic Agent. O. B. Crawford, C. Brasher, P. Ottosen and W. W. Buckingham.—p. 1073.
- Teaching of Social Medicine: Who Will Bell the Cat? H. A. Kemp.—p. 1076.

Hypercholesterolemia.—In a general medical practice 822 unselected patients, including men and women from the second to the ninth decades of life, were studied for the purpose of establishing the relationship of blood cholesterol levels to age, sex, blood pressure, basal metabolism, and various disease states. Of the 822 patients, 554 showed no significant disease states known to be associated with a change in cholesterol values. They served as the "normal" group for the study. These patients were arranged in age groups by decades in an attempt to establish a practical norm with which the blood cholesterol level of any person might be compared. The sex differential was observed to be of no practical significance. Determination of blood cholesterol levels in the normal group revealed a range of the levels from 112 to 438 mg. per 100 cc. The mean average cholesterol level for all ages was 228 mg. per 100 cc., with a standard deviation of plus or minus 41.6. An analysis of the mean average cholesterol levels in the age groups revealed a progressive increase in values with advancing years to a point between the ages of 50 and 60, at a mean age of 53.7 years, and a decline in cholesterol values in the later decades. Individual blood cholesterol levels should be compared with the mean average blood cholesterol levels for the age groups in determining the normal status of a particular level. The 268 patients rejected from the normal group because of the presence of disease states, had blood cholesterol levels conforming to the levels reported in the literature for these diseases. Of these 268 patients, 142 classified as having myocardial disease presented an age-group curve similar in configuration to the "normal" age group curve. The increase in the mean average cholesterol levels in the former group with increasing age was comparable to the increased clinical incidence of the degenerative diseases in the older age groups. The presence of a high blood cholesterol level unexplained by an obvious disease requires more complete and prolonged study to establish the significance of the abnormality. A high cholesterol level may be considered an abnormal cholesterol level until proven otherwise.

Mastectomy in Carcinoma of the Breast.—Of 84 patients with microscopically proven cancer of the breast, 54 were treated by radical mastectomy, followed by x-ray therapy in those with axillary node metastases, while 30 patients were subjected to simple mastectomy followed by x-ray therapy. Of the patients with radical mastectomy, 24 are still alive, a survival rate of 44.4%, and six of those now dead lived longer than five years postoperatively, a five-year survival rate of 54.7%. Using Cade's modification of Portmann's original classification, the survival rate for patients with Stage 1 lesions was 81.2% (13 of 16); for Stage 2, 48.4% (16 of 33). None of the five patients with Stage 3 lesions lived as long as five years, and no patient with Stage 4 lesions was treated by radical mastectomy. These results compare favorably with those reported by other clinics. Of the 30 patients treated with simple mastectomy plus postoperative

Irradiation, 15 are now alive, a survival rate of 50%. Of the 15 dead, 4 lived longer than five years, a five-year survival rate of 63.3%. Simple mastectomy yielded a 91.6% (11 of 12) five-year survival rate for Stage 1, and a 77% (7 of 9) five-year survival rate for Stage 2 lesions. Patients with Stage 3 lesions had a survival rate of 16.7% (1 of 6) and none of the patients with Stage 4 lesions lived as long as five years. These results indicate that simple mastectomy offers a better prognosis than radical mastectomy. The authors admit that their series is quite small, but they believe that until larger series are available, the cumulative data from such small series must suffice for temporary evaluation of the McWhirter type of therapy.

Surgery, Gynecology and Obstetrics, Chicago

93:529-656 (Nov.) 1951

- The Present Story on Battle Casualties from Korea: Six Months' Study. W. F. Bowers, F. T. Merchant and K. H. Judy.—p. 529.
- Standard Contact Burn: Method of Production and Observation on Blood Picture Following Its Production in Dogs. J. W. Brooks, P. Robinett, T. L. Largent and E. I. Evans.—p. 543.
- Ileostomy for Ulcerative Colitis: Technique, Complications, and Management. R. Warren and L. S. McKittrick.—p. 555.
- Treatment of Edema of Arm. W. T. Foley.—p. 568.
- Chronic Thyroiditis: Supravital Studies of Surgical Goiter Specimens. V. E. Chesky, W. C. Drees and C. A. Hellwig.—p. 575.
- Evaluation of Preoperative Skin Preparation. J. J. Murphy, J. A. Dull, J. Gamble and others.—p. 581.
- Aberrant Systemic Arteries to Lower Lung. F. H. Cole, F. H. Alley and R. S. Jones.—p. 589.
- Rectocolic Anastomosis: Simplified Method. E. D. Sugarbaker and H. M. Wiley.—p. 597.
- Method of Closing Defects in Bowel. E. J. Poth and R. G. Martin.—p. 606.
- Ectocervix During Gestation. J. J. Nolan and O. J. Pollak.—p. 609.
- Effect of Bantline, Vagotomy, and Subtotal Gastrectomy upon Pancreatic Secretion. J. R. Thistlethwaite.—p. 616.
- Pancreatic Injuries: Experimental Study. H. L. Popper and H. Necheles.—p. 621.
- Studies on Vagotomy in Treatment of Peptic Ulcer: V. Clinical and Physiologic Results Three to Four Years After Surgery. I. F. Stein Jr. and K. A. Meyer.—p. 625.
- Major Surgery in Hodgkin's Disease. R. D. Williams, N. C. Andrews and R. P. Zanes Jr.—p. 636.

Chronic Thyroiditis.—During the last 10 years Chesky and associates observed 169 cases of chronic thyroiditis among 2,031 patients requiring thyroidectomy, an incidence of 8.3%. The 169 cases included 8 cases of Riedel's struma (fibroplastic form), 146 cases of Hashimoto's disease (lymphadenoid goiter), 9 cases of giant cell thyroiditis of DeQuervain, and 6 cases that could not be classified, representing the earliest stages of chronic thyroiditis. The authors present the results of their supravital studies that led to a new concept of the etiology of chronic thyroiditis. In most of the 54 goiters examined they found large cells containing coarse salmon-red granules in the cytoplasm. In 30 specimens these large cells were found within the lumen of follicles; in 18 goiters they were seen in the interfollicular tissue. These cells were macrophages, and to determine the significance of these macrophages the authors studied paraffin sections of thyroids showing chronic inflammation. On the basis of their investigations they stress the following points: 1. Small foci of chronic thyroiditis characterized by aggregations of lymphocytes are common in exophthalmic and nodular goiters (63.9%) and not infrequent in normal-sized thyroids obtained by autopsy (16.2%). 2. There are only quantitative differences between the severe grades of chronic thyroiditis (Riedel's, Hashimoto's, and DeQuervain's type) and localized foci of chronic thyroiditis in exophthalmic goiter and nodular goiter. 3. All attempts to find bacteria or a virus as the cause of chronic thyroiditis have been unsuccessful. 4. Supravital studies of fresh surgical material suggest a new concept of the cause of this disease. By change in the composition of colloid, macrophages are attracted that invade the lumen of follicles, ingest colloid, and return into the interfollicular stroma. If they disintegrate in the stroma the liberated colloid attracts lymphocytes that cluster around the colloid and produce the anatomical picture of chronic thyroiditis. Excess thyrotropic hormone seems the most important factor in the causation of the colloidal changes responsible for the attraction of the macrophages. 5. The new concept of chronic thyroiditis as a chemical inflammation—comparable to lipogranuloma—is supported by experimental, supravital, and electronmicroscopic findings.

Vagotomy in Peptic Ulcer: Late Results.—Two important questions remain to be answered before vagotomy can be evaluated finally. It must be ascertained (1) what proportion of patients operated on continue to have unpleasant symptoms or have a recurrence of ulcer symptoms after a number of years; (2) whether the marked decrease in gastric secretory capacity and motility found in the early postoperative period is permanent. A total of 40 patients were followed for from 28 to 50 months. The clinical results in these 40 patients were good in 26, fair in 10, and poor in 4. The patients were subjected to physiologic tests and three types of response are differentiated: (1) normal vagus function, (2) partial vagus function, and (3) no vagus function. No significant change in the gastric secretory or motor activity is present in patients with normal vagus function following surgery. Reduction in the motility and in both spontaneous and stimulated acid secretion of the stomach is demonstrated in patients with partial vagus function and those with no vagus function three to four years after vagotomy. This reduction is greatest in patients with no vagus function. No evidence of any return of gastric activity is present in this group. A slight return of acidity is found in patients with partial vagus function as determined by the basal secretion; however, in spite of this, there is still a marked decrease in comparison with the preoperative level. The previous failure to recognize the existence of the intermediate group (partial vagus function) probably accounts for reports concerning the lack of correlation between the physiologic and therapeutic effects of vagotomy. The response of patients with partial vagus function to insulin hypoglycemia is delayed, and may be undetected unless observation is continued for at least two and a half hours after the injection of insulin. Spontaneous secretion of free hydrochloric acid during the night or basal secretion indicates vagus function. In addition, vagal type motility, either spontaneous or subsequent to hypoglycemia, indicates vagus function. Decrease in gastric motor and secretory activity following vagotomy in patients with partial vagus function and no vagus function remains three to four years after vagotomy.

Wisconsin Medical Journal, Madison

50:1065-1156 (Nov.) 1951

- Essential Treatment of Major Burns. A. R. Mailer.—p. 1088.
- Treatment of Vasospastic Conditions with Bently Hydrochloride: Preliminary Report. D. C. Ausman and J. J. Arneith.—p. 1089.
- Effect of Ammonium Chloride on Clinical Pattern and Electroencephalogram in Epilepsy: Preliminary Report on New Addition to Therapeutic Armamentarium in Epilepsy. F. Kant and W. E. Gilson.—p. 1095.
- Bantline in Treatment of Peptic Ulcer. J. Shaiken.—p. 1099.
- Subtotal Gastrectomy: Analysis of 147 Consecutive Cases. W. M. Kearns Jr.—p. 1101.
- *Silage Gas Poisoning: Case Report. G. A. Fostvedt.—p. 1103.

Silage Gas Poisoning.—The case is reported of a man who entered a previously closed silo. He cried for help, but a few minutes later was found in an unconscious state. Examination revealed arrhythmia, slow and shallow respiration, absence of reflexes, and occasional twitchings of the facial muscles. The patient did not respond to pain stimuli or the spoken voice. The pupils were dilated. The patient appeared to be anesthetized. He was given oxygen and respiratory stimulants, such as ammonia inhalations, injections of nikethamide (coramine®), camphor, and caffeine and sodium benzoate. Strophanthin was given for the cardiac embarrassment. Consciousness was restored after about one hour, but abdominal cramps persisted for another hour; arrhythmia persisted and he had a headache, but slept well the next night and felt well the following morning. He reported that he had become faint and had lost muscular coordination within one-half minute after climbing into the silo. The accidental anesthesia and toxic reactions presumably were due to carbon dioxide from silage fermentation. Carbon dioxide formation occurs also in beet sugar manufacture, yeast production, in wine vats, in linseed oil production, in brewery vats, and from dry ice. To prevent acute intoxication from silage gas, the silo area should be ventilated prior to entering it, and the atmosphere should be tested with a candle flame or a small animal, such as a bird or a mouse.

FOREIGN

Acta Chirurgica Scandinavica, Stockholm

102:167-240 (No. 3) 1951. Partial Index

Surgical Treatment of Wide Patent Ductus Arteriosus. P. Sandblom and G. Ekström.—p. 167.

*Double Aortic Arch. G. Ekström and P. Sandblom.—p. 183.

Post-Operative Changes in Circulation and Effects of Oxygen Therapy. L. Troell.—p. 203.

On Catgut Tetanus and Sterility of Catgut. T. Savolainen.—p. 215.

Double Aortic Arch.—A double aortic arch is reported in two girls, who were operated on at the age of 5 years and 2 months, respectively. Left thoracotomy with subperiosteal resection of the fourth rib, performed according to Crafoord's method in both cases, provided an excellent approach. In the older girl both arches were of the same diameter. The ligamentum arteriosum was cut and division of the left aortic arch and suture was performed according to Gross' technique. The postoperative course was uneventful and symptoms of compression or infection of the respiratory tract did not recur after the operation. In the second case, the diameter of the left arch was much smaller than that of the right. Division of the left arch was first carried out between double ligatures. The left subclavian artery also was divided, and only then did the posterior part of the left arch slip to the right behind the esophagus so that the vascular ring opened. Immediately after operation the patient had no respiratory symptoms, but laryngeal stridor reappeared within 12 hours, necessitating tracheotomy. A review is presented of 83 cases of double aortic arch reported in the literature. Of these 83 patients, 43 presented symptoms of compression from a vascular ring. Division of the compressing vascular ring, including division of the ligamentum arteriosum and ductus arteriosus, was adequate surgical treatment in 29 cases. There were six postoperative deaths. From their experience in two cases and data from the literature the authors draw the following conclusions: congenital respiratory stridor may suggest double aortic arch, and roentgenologic examination of the trachea and esophagus should be made with the aid of a water-soluble contrast medium such as 35% aqueous solution of iodopyracet ("umbradil"). Children with severe symptoms of compression not given surgical treatment usually die within the first seven months of life. Children with mild symptoms of compression may, despite continual pulmonary complications, occasionally survive with conservative treatment in the form of prophylaxis against infection and chemotherapy of bronchopneumonia. The ductus arteriosus should as a rule be approached from the left side. Right thoracotomy is preferred when preoperative roentgenograms reveal a left aortic knob and a large retroesophageal vessel. Double aortic arch with symptoms of tracheal obstruction from compression indicates surgical intervention. If symptoms are mild, operation may be postponed until the child is one-year-old. In the absence of compression surgical treatment is not indicated.

Annales Medicinae Internae Fenniae, Helsinki

40:99-196 (No. 2) 1951. Partial Index

Pulmonary Mycosis: Clinical and Pathological Features. R. Elo, R. Päätilä and V. Ritama.—p. 99.

Essential Thrombocytopenia and Pregnancy: Report of Case. E. Helske.—p. 117.

Electrocardiographic Observations on 650 Finnish Athletes. E. Klemola.—p. 121.

Inflammatory Vascular Changes in Coronary Disease. V. Ritama, H. Laitinen and M. Virkkunen.—p. 133.

*Coarctation of Thoracic Aorta with Dissecting Aneurysm Distal to Obstruction: Review of Literature and Report of Case. E. Taipale and Per-Erik Heikel.—p. 187.

Coarctation of Thoracic Aorta with Aneurysm.—A study of the literature revealed 26 cases of coarctation of the aorta with associated aneurysm of the descending aorta distal to the obstruction. In 21 cases the patients died at an average age of 29 years, the cause of death being rupture of the aneurysm in 14. Three patients had borne children. A case is reported of a woman, aged 52, in whom coarctation of the aorta with an aneurysm distal to the obstruction was diagnosed during life. She had had two children. This patient died of myocardial infarction, and at autopsy a dissecting aneurysm was found. Histological examination showed marked calcification of the aortic aneurysm.

Annales Paediatrici, Basel

177:277-328 (Nov.) 1951

*Administration of PAS by the Lumbar Route in the Course of Combined Treatment of Tuberculous Meningitis. M. H. Beguin.—p. 277.

The Morgagni-Adams-Stokes Syndrome in Diphtheria. E. Hausmann.—p. 294.

Studies on the Concentration of Free Amino-Acids in Infants and Children. J. Ströder, H. Grunhofer and W. Engel.—p. 304.

Heredity in Infantile Type of Gaucher's Disease. E. Stransky and T. L. Conchu.—p. 319.

p-Aminosalicylic Acid in Tuberculous Meningitis.—Combined treatment of tuberculous meningitis with streptomycin and p-aminosalicylic acid ("PAS") minimizes the development of bacilli resistant to streptomycin. Bacteriostatic action of the two is additive, making it possible to use streptomycin in nontoxic doses. p-Aminosalicylic acid given only by mouth enters the cerebrospinal fluid in quantities generally too small to be effective; the proportion required in vitro ranges between 25 γ and 300 γ per 100 cc. The concentration varies, depending apparently on the albumin content of the cerebrospinal fluid. Two methods of obtaining an adequate concentration have been employed: (1) intravenous infusion by continuous drip, making it possible to give 40 gm. daily without the digestive disturbances that arise when the adult dose of 14 gm. is exceeded in oral administration; and (2) combined p-aminosalicylic acid and streptomycin given intrathecally. The second method was used with certain modifications in 10 cases. The author gave streptomycin and p-aminosalicylic acid intrathecally, with dihydrostreptomycin intramuscularly and p-aminosalicylic acid orally. Results obtained (7 patients apparently cured and 1 improved) were better than with streptomycin alone or combined with the acid given orally. Tolerance for the combined medication was excellent. A 5% solution of p-aminosalicylic acid is isotonic and has a pH of about 7, so that irritation due to acid reaction need not be feared. Doses of 3 mg. per kilogram of body weight given intrathecally were resorbed in 24 hours to the extent of from 100 to 600 γ per cent. One injection a day sufficed, because contact with bacteriostatic doses for several hours daily will arrest multiplication of the tubercle bacillus. Lumbar intrathecal injections should be continued for about six months to prevent relapse. The action of streptomycin and p-aminosalicylic acid is bacteriostatic and not bactericidal; definitive cure is obtained only when an impassable barrier has been built up around the bacilli that survive in the inflammatory meningeal lesions. The following scheme of treatment is suggested: intrathecally—streptomycin, at first 2 mg. per kilogram of body weight, then 1 mg., and the sodium salt of p-aminosalicylic acid, 3 mg.; intramuscularly—dihydrostreptomycin, at first 40 mg. per kilogram of body weight, later 20 mg.; orally—p-aminosalicylic acid, 0.25 to 0.3 gm. Lumbar punctures are made daily for one month, three times a week for two months, twice a week for two months, and finally once a week for one month. The concentration of the acid in the cerebrospinal fluid should be determined regularly, 200 to 300 γ per 100 cc. after 24 hours being sufficient. The 5% solution of sodium salt of p-aminosalicylic acid and the streptomycin are diluted with a physiological solution up to 5 to 10 cc. and given in the same syringe. The concentration of the acid solution should not exceed 1% (10 mg. per cubic centimeter) when given intrathecally. Dosage is adapted to each child; the number of punctures may be increased or decreased. Disturbance of hearing does not follow this dosage.

Beiträge zur Klinik der Tuberkulose, Heidelberg

106:91-182 (No. 2) 1951. Partial Index

Clinical Considerations Concerning Treatment of Miliary Tuberculosis of Lungs and Tuberculous Meningitis with Streptomycin. H. G. and M.-L. Schikarski.—p. 93.

Absorption Increasing Effect of Hyaluronidase on Inhalation of Tuberculous Substances. A. Lass.—p. 104.

Preliminary Results of Chemotherapy of Pulmonary Tuberculosis with Respect to Transmission of Contagious Diseases. C. Götsch.—p. 113.

*Inhalation Therapy with Antibiotic Substances. T. Lammers and K. Herold.—p. 158.

Inhalation Therapy with Antibiotic Substances.—Satisfactory results from inhalation therapy with antibiotics depend on use of a suitable nebulizer, maintenance of therapeutic concentrations of the drugs in the lung tissues over prolonged period

and knowledge of the sensitivity of the bacterial content of the sputum. Therapeutic concentrations were maintained in the lung tissues for at least four and nine hours when 100,000 and 500,000 units of penicillin G, in 5 cc. of distilled water, were administered by aerosol inhaler. Therapeutic concentrations of ampicillin, streptomycin, and terramycin were maintained in lung tissues for 12 to 14 hours by the administration of mg. of each of these antibiotics in aerosol form. Because of the rapid absorption of penicillin by the lung tissues a therapeutic level of this antibiotic was maintained in the blood for 2 to 4 hours after inhalation of 100,000 units of penicillin for seven to nine hours after inhalation of 500,000 units of ampicillin. Streptomycin, aureomycin, and terramycin were absorbed by the lung tissues more slowly and in smaller amounts than penicillin, and therapeutically effective blood levels were obtained when these antibiotics were administered by inhalation. The plasma concentration of penicillin was increased and its duration in the plasma was shortened by the addition of opylarterenol ("aludrine") to the aerosol. Hyaluronidase added to the aerosols caused liquefaction of necrotic lung tissue without impairing absorption of antibiotics. A pronounced decrease of bacteria in the sputum resulted from inhalation of antibiotics. With prolonged penicillin inhalation therapy the number of penicillin-resistant bacteria (particularly coliform bacteria and yeasts) in the sputum increased. After two to three days of streptomycin aerosol treatment the same number of phytic bacteria were observed in the sputum following an initial reduction as had been observed previously, but all types of bacteria had become completely resistant to the usual therapeutically effective concentrations of streptomycin. The number of bacteria in the sputum remained low, even with prolonged ampicillin and aureomycin inhalation therapy, and the bacteria in the sputum did not become resistant to these antibiotics.

British Journal of Dermatology, London

63:343-388 (Oct.) 1951

Circulation of Generalized Erythrodermia with Superficial Lymphadenopathy (Lipomelanin Reticulosis). A. Jarrett and H. S. Kellett.—p. 343.
63:389-430 (Nov.) 1951

Genital Syphilis in One of Twins. T. James.—p. 389.
Diagnosis of Sarcoidosis with Erythrodermic Lesions: Treatment with Calomel. J. E. M. Wigley and L. A. Musso.—p. 398.

British Journal of Ophthalmology, London

35:509-572 (Sept.) 1951

Diagnosis and Management of Paralysis of Extrinsic Ocular Muscles: A Special Reference to Surgical Treatment in 219 Cases. T. K. Ryle and A. G. Cross.—p. 511.
Ampicillin in Trachoma. J. W. R. Sarkies.—p. 549.
Intra-Microscopic Study of Infective Agent of Trachoma. Y. Itô, M. Itô and Y. Sasaki.—p. 553.
Retinal Micro-Aneurysms in Connection with Generalized Diseases Causing Retinopathy. R. Syssi.—p. 560.

British Medical Journal, London

2:1167-1232 (Nov. 17) 1951

Experimental Approach to Problem of Diabetes Mellitus. F. G. Young.—p. 1167.
Hyaluronidase Skin Spreading Effect: Analysis of Repeated Measurements. E. J. Holborow and M. K. Keech.—p. 1173.
Constitution of Dermal Barrier to Dye Spread After Hyaluronidase Injection. E. G. L. Bywaters, E. J. Holborow and M. K. Keech.—p. 1178.
Eosinophilic Response to Cortisone and A.C.T.H. in Normal Subjects. H. Kellgren and O. Janus.—p. 1183.
Eosinophil Counting: Modification of Pilot's Method. J. C. W. Macfarlane and G. W. Cecil.—p. 1187.
Wilson's Disease with Associated Polyarthritides: Aetiological Study of Arthritis Syndrome. J. E. Coughley and J. E. McCoy.—p. 1189.
Penicillin Treatment of Acute Mastoiditis in Children. J. I. M. Black.—p. 1191.
Effect of Myxoedema Developing During p-Aminosalicylic Acid Therapy. M. Komrower.—p. 1193.
Test for Differentiating Uterine from Extrauterine Complications of Pregnancy and Puerperium. N. Alders.—p. 1194.

Eosinopenic Response to Cortisone and Corticotropin.—The eosinopenic responses to single doses of 6.25, 12.5, 25, 50, and 100 mg. of cortisone given orally and to single doses of 2.5, 5, 10, 20, 40 and 100 mg. of corticotropin (ACTH) given intra-

muscularly were studied in four normal men between the ages of 32 and 43. A modification of Dunger's technique was used for estimating the number of circulating eosinophils. Results showed that the time relations of the responses to these two drugs were remarkably similar, but the individual responses to either cortisone or corticotropin, or both, varied considerably. The eosinopenic response to various corticotropin preparations and to acute febrile stress induced by intravenous administration of 10 ml. of typhoid-paratyphoid (T. A. B.) vaccine were also compared, and throughout these studies the differences in individual responses were maintained. The number of circulating eosinophils was also studied during periods of stress from established panhypopituitarism in three patients who showed an exaggerated and prolonged eosinopenic response to cortisone given orally. Although many factors may influence eosinopenic responsiveness, it is suggested that the eosinopenic response of the individual to 50 mg. of cortisone administered orally, in addition to the corticotropin response test, might provide a useful guide to therapy with these hormones, and might indicate the activity of the pituitary-adrenal mechanism.

Penicillin in Acute Mastoiditis.—Of 118 children with acute mastoiditis treated with penicillin, 59 who did not have fluctuation recovered without surgical intervention. The remaining 59 patients had fluctuation, and in 38 of them the postauricular abscess had to be incised. In the other 21 the abscess was absorbed spontaneously. Only three patients required mastoidectomy, and one of them had tuberculous tympanomastoiditis. The dose of penicillin recommended is 300,000 units daily by intramuscular injection. Routine treatment of acute mastoiditis in children by penicillin injections is advocated. Once the penicillin treatment has been instituted, the patient should be examined daily. A rapid improvement in the general condition and temperature is to be expected. In a few days the postauricular swelling should show a reduction in size. When fluctuation is detected, if the abscess remains the same size for 24 hours it should be incised. If otorrhea is present and does not cease in about seven days, the pus should be examined for penicillin-resistant organisms, and appropriate action taken. Penicillin treatment should be continued until the tympanic membrane regains a normal texture and the tympanum contains air. All patients should be followed for about three months to be sure that hearing returns and that recovery is not retarded by factors such as enlarged tonsils and adenoids or sinusitis.

Edinburgh Medical Journal

58:457-520 (Oct.) 1951

*Survey of Granite Industry in Aberdeen with Reference to Silicosis. A. Mair.—p. 457.
Prognosis in Pulmonary Tuberculosis in Aberdeen and Aberdeenshire. R. Fraser.—p. 481.
Fatality and Survivorship in Pulmonary Tuberculosis: Study of Notified Cases in Edinburgh: 1936-44. M. S. Acker.—p. 489.
*Bronchiectasis Treated with Chloramphenicol. N. Wynn-Williams and E. N. Moyes.—p. 503.
Lymphosarcoma Terminating with Leukaemia. W. R. Gauld.—p. 507.

Silicosis in the Granite Industry.—The dread of silicosis in the Aberdeen granite industry has made it difficult to obtain sufficient workers. Parents wished to prevent their boys learning a trade that, they believed, would cause early death from "mason's disease." Mair initiated this survey in 1948 in an attempt to determine the incidence of this disease in the industry. Of approximately 1,500 men working with granite, 521 were employed in some capacity involving a dust hazard, and 510 of these submitted to x-ray examination. Of these, 56 showed radiological evidence of silicosis. However, in 35 the silicosis was of a minor degree without other signs or symptoms. Silicosis severe enough to entitle the worker to receive disablement benefit was found in only 11. The mean ages of workers with four increasing degrees of silicosis (graded roentgenologically) were 53.7, 59.4, 63.2, and 65.4, respectively, while the corresponding mean "dust-years" necessary to produce these lung changes were 32, 38, 40, and 42. The findings in men at work and those retired, reveal that, while silicosis exists to a moderate extent, it commences so late in life and progresses so slowly that many stonecutters live

to comparative old age and die of other diseases. The incidence of tuberculosis in the men at work was found to be no higher than one would expect in the community at large. It is suggested that the high number of deaths among stonecutters in Aberdeen during the early part of the century registered as "phthisis" was actually due to tuberculosis and not to silicosis alone or silicosis complicated by tuberculosis.

Bronchiectasis Treated with Chloramphenicol.—The treatment of bronchiectasis with penicillin, by intramuscular injection and in the nebulized form, in some cases combined with streptomycin therapy, reduced the amount of sputum by an average of 61%. Since this treatment required hospitalization, Wynn-Williams and Moyes decided to try chloramphenicol administered by mouth, which had proved successful in treatment of three hospitalized patients with severe bronchiectasis. The authors chose 12 ambulatory patients for treatment with chloramphenicol either because they were known to have had sufficient sputum to have required previous treatment in the hospital, or because they stated their sputum was enough to cause inconvenience. Eight received treatment for five days, three had treatment for eight days, and in one the drug was stopped on the third day after only 7 gm. had been given because of side-effects. The sputum was reduced by an average of 83%, being entirely eliminated in four and rendered mucoid in eight. Compared with previous antibiotic treatment, chloramphenicol appeared to be more effective in four patients and equally effective in two. This result is noteworthy, since it was obtained in outpatients who continued normal activity. Probably the sputum will gradually increase, as following penicillin therapy, and some increase occurred in several patients within a few weeks. It is not claimed that chloramphenicol will remove permanently the infection in dilated bronchi, but, if these results can be repeated, a valuable antibiotic has been added to the therapeutic armamentarium.

Geburtshilfe und Frauenheilkunde, Stuttgart

11:771-866 (Sept.) 1951. Partial Index

- Improvement in Irradiation Therapy in Advanced Cases and in Recurrences of Carcinoma of Cervix. R. K. Kepp.—p. 771.
- *Incidence of Congenital Defects and Age of Mother. H. Hegnauer.—p. 777.
- Intrauterine Death of Fetus and Toxoplasmosis. W. Döntenwill.—p. 792.
- Cytologic Diagnosis of Primary Tubal Carcinoma from Vaginal Smear. G. Besserer.—p. 804.
- Cytologic Findings in Cervical Smears in Presence of Endometritis and Tuberculous Cervicitis. H. Cramer.—p. 809.

Incidence of Congenital Defects and Age of Mother.—With data on 140,000 births, studies were made of the relationship between incidence of congenital deformities and age and parity of the mother. Women who gave birth between the ages of 36 and 40 had twice as many and those over 40 three times as many deformed children as did younger mothers. The incidence of developmental disturbances was higher with increasing numbers of pregnancies, but not as high as in relation with the age of the mother. Therefore it was concluded that the higher incidence in congenital deformities in this group was also the result of the higher age of the mother. The relation of incidence and age was not equal in all types of deformities. The incidence of defects in the extremities, genitalia, and facial clefts was not related to maternal age. However, defects in the central nervous system, such as mongolism, hydrocephalus congenitus, and anencephalus, showed a decided relation to the age of the mother, but surprisingly this was not true of deformities of the spinal cord. Studies of congenital goiter suggested that not only the mother's age but also the number of pregnancies determined the incidence.

Journal of Tropical Medicine and Hygiene, London

54:221-242 (Nov.) 1951

- Assessment of Value of Cholera Vaccine as Used in Single Dose Mass Inoculation. L. Kant.—p. 223.
- Toxoplasmosis. E. W. Hart, J. W. Paulley, J. S. Rivers and E. K. Westlake.—p. 226.

Lancet, London

2:845-894 (Nov. 10) 1951

- Vascular Spasm. G. W. Pickering.—p. 845.
- Fluid Balance in Congestive Cardiac Failure: Two Mechanisms in Diuretic Treatment. T. E. Lowe.—p. 851.
- *Chronic Mercury Poisoning in Men Repairing Direct-Current Meters. P. L. Bidstrup, J. A. Bonnell, D. G. Harvey and S. Locket.—p. 851.
- Pantothenic Acid in Paralytic Ileus. J. E. Jacques.—p. 861.
- Successful Transfusion of Previously Frozen Human Red Cells. P. Mollison and H. A. Sloviter.—p. 862.
- Pulmonary Embolism After Treatment with Heparin. R. M. Cadenhead.—p. 865.
- Potential of Antibacterial Activity of Sulphathiazole by Glutathione. G. C. Ware.—p. 865.

Mercury Poisoning in Men Repairing Direct-Current Meters. Five men who were employed in workshops where direct-current (D. C.) electric meters were repaired were found to have chronic mercury poisoning. To determine the incidence of chronic mercury poisoning in this industry, men employed as meter repairers in the London area were examined. Arrangements were made for clinical examination of the exposed men and estimation of mercury excreted in the urine in 24 hours, estimation of mercury present in the atmosphere in each workshop. Of the 161 men examined, 103 repaired D. C. meters, 58 tested these meters or repaired alternating-current (A. C.) meters. Although there is no direct contact with mercury in the latter work, it is sometimes done in the same workshops where D. C. meters are repaired, and the men are therefore exposed to mercury in the atmosphere. Symptoms or signs of chronic mercury poisoning were found in 27 men, all of whom repaired D. C. meters. No case of chronic mercury poisoning was detected among 58 men who tested meters or repaired A. C. meters. In doubtful cases the diagnosis was confirmed by estimating the amount of mercury excreted in the urine. The excretion of more than 300 γ of mercury in 24 hours was usually accompanied by symptoms of chronic mercury poisoning, which in some cases had been attributed to neurosis. The concentration of mercury in the working atmosphere was much higher during the winter months, except where exhaust ventilation had been installed. The incidence of mercury poisoning varied according to the concentration of mercury in the working atmosphere. Measures to prevent mercury poisoning are suggested.

2:895-946 (Nov. 17) 1951

- The Arts of Medicine and Their Future. F. M. R. Walshe.—p. 895.
- *Treatment of Hypertension with Hexamethonium Bromide. E. J. Murphy.—p. 899.
- Action of Dehydro-Ascorbic Acid and Alloxan on Tuberculin-Sensitivity in Guinea-pigs. D. A. Long, A. A. Miles and W. L. M. Perry.—p. 903.
- *Toxoplasma Infection in English Children: Survey with Toxoplasma Intradermal Antigen. O. D. Fisher.—p. 904.
- Microchromatographic Method for Separation of Certain Fraction 17-Ketosteroids in Human Urine. M. H. Pond.—p. 906.
- Chronic Osteomyelitis Treated by Primary Closure with Antiseptic Control. A. K. Basu.—p. 909.
- Typhoid Osteomyelitis Treated by Surgery and Chloromycetin. J. Morgan.—p. 911.
- Low Plasma-Potassium Levels in Acute Leukaemia. A. Videbaek.—p. 913.
- Antiglobulin (Coombs) Test in Brucellosis. M. M. Wilson and E. J. Merrifield.—p. 913.
- Recovery of Newborn Child from Bact. Coli Meningitis. J. S. Ebsworth and D. G. Leys.—p. 914.

Hexamethonium Bromide in Hypertension.—Murphy has used hexamethonium bromide in treatment of 43 patients with various degrees of hypertension. The drug was given orally or subcutaneously, but whenever possible the oral route was used for ease of administration. When the drug was unsuccessful orally, it was given parenterally. Some of the patients had previously been treated without success by sympathectomy or potassium thiocyanate. Results obtained with hexamethonium bromide were encouraging. The most dramatic improvements were seen in patients with severe retinopathy and placid temperament. The nature and properties of the hypertension must be determined before treatment is decided on. Possible side-effects mentioned and measures to counteract them are outlined. It has been suggested that long-term improvement is due solely to the bromide ion, but reasons are given why this explanation is not acceptable. Satisfactory preliminary results obtained with hexamethonium bitartrate are mentioned.

Toxoplasmosis in English Children.—Toxoplasmosis is now recognized as a disease of world-wide distribution. In the commonly recorded form the infection is congenital and may be characterized by hydrocephalus, cerebral calcification, and choroidoretinitis. The acquired infection has been recognized in several clinical forms; in children it occurs as a nonsuppurative meningoencephalitis, and in adults as an enteric or rickettsial type of illness. However, the infection may be revealed only by the presence of toxoplasma antibodies in the serum. To determine the incidence of toxoplasma infection in English children, their sensitivity to intradermal inoculations of toxoplasmin was used like the tuberculin reaction in tuberculosis. The preparation of the toxoplasmin antigen and results of intradermal inoculation are described. A large-scale survey of children by this method was correlated with serological investigation of toxoplasma antibodies by the dye test and the complement-fixation test. The incidence of infection was found to be insignificant in the earliest age group (up to 4 years), rising to 7% in the third age group (10 to 14 years), and to 17.5% in the adult group (15 years or more). It is concluded that toxoplasmin reaction is a reliable means of detecting toxoplasma infection in population surveys and as a screening test for suspected cases.

Medical Journal of Australia, Sydney

2:485-516 (Oct. 13) 1951

- Influence of Intrathecally Administered Adrenaline on Adrenal Cortex. S. Rose.—p. 485.
Perineal Dissection in Excision of Carcinoma of Rectum. E. S. R. Hughes.—p. 499.
Use of Skin Grafting in Hernial Repair. J. C. B. Allen.—p. 502.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

95:3017-3080 (Oct. 13) 1951. Partial Index

- *Dupuytren's Contracture and Epilepsy. W. Kramer and J. Luten.—p. 3023.
Acanthosis Nigricans. A. R. F. Somers.—p. 3029.
A Case of Infectious Mononucleosis Transmitted by Blood Transfusion. J. F. deVos and F. H. Kuipers.—p. 3036.

Dupuytren's Contracture and Epilepsy.—Kramer and Luten examined 554 epileptic patients for the presence of Dupuytren's contracture and detected this form of fibrosis in 38 or 7%. This incidence is not as high as that reported by other investigators (40% and 52%), but over half of the epileptics studied were less than 20 years old. Among 50 epileptics between 40 and 50 years of age there were 11 (or 22%) with Dupuytren's contracture and among 31 between 50 and 60 there were 9 (29%). The authors had previously observed that Dupuytren's contracture is often associated with other connective tissue lesions. Since Scandinavian authors had stated that such associated lesions were particularly frequent in epileptics, the authors list the incidence of Dupuytren's contracture and knuckle pads, plantar fibroma, and humeroscapular periarthrosis, which were relatively frequent. The authors feel that the increased incidence of Dupuytren's contracture in epileptics is related to the prolonged use of large doses of barbiturates rather than to the epilepsy. In some cases trauma may be a factor. The authors gained the impression that epileptics with Dupuytren's contracture are of a constitutional type, with signs of status dysraphicus. It is assumed that this constitutional anomaly favors the development of Dupuytren's contracture.

Nordisk Medicin, Stockholm

46:1437-1476 (Sept. 26) 1951. Partial Index

- Fractures of Malar Bone. T. Skoog.—p. 1440.
*Curare in Abdominal Surgery. A. Lidström and S. O. Liljedahl.—p. 1445.
Result of Osteosynthesis with Modified Nail in Fractures of Mid-Neck of Femur. A. Ekengren.—p. 1449.
Acute Atrophy of Bones of Shoulder Joint: Osteoarthropathy in Syringomyelia. M. Hauge.—p. 1450.

Curare in Abdominal Surgery.—On the basis of their use of curare in conjunction with "narkotal" (an intravenous barbiturate) and nitrous oxide or ether in 692 abdominal operations, Lidström and Liljedahl conclude that curare is a valuable adjunct to anesthesia in all intra-abdominal surgery. The frequency of complications during and after operation is low. The use of

curare at the beginning of ether anesthesia offers several advantages. Curare during ether anesthesia should be administered in small doses (1.5 to 3 mg.). Administration of curare in the final stage of anesthesia is cautioned against, as it apparently increases the risk of postoperative complications. Curare anesthesia should always be administered by personnel fully experienced in anesthesia and familiar with endotracheal intubation.

Practitioner, London

167:305-470 (Oct.) 1951. Partial Index

- The Changing Face of Medicine 1868-1951. H. Dale.—p. 309.
Social Background of Medicine. H. Bashford.—p. 315.
Trends of General Practice: Hundred Years in Yorkshire Dale. W. N. Pickles.—p. 322.
Advances in Medicine. H. Cohen.—p. 330.
Advances in Surgery. D. C. Balfour.—p. 343.

167:471-572 (Nov.) 1951. Partial Index

- Treatment of Acute Otitis Media. J. P. Monkhouse.—p. 475.
Infections of Outer Ear. E. G. Collins.—p. 481.
Problems of Chronic Running Ear. A. B. Thomas.—p. 491.
Treatment of Otosclerosis. T. Cawthorne.—p. 499.
Use and Limitation of Hearing Aids. F. C. Ormerod.—p. 504.
Sociological Aspects of Deafness. R. S. Stevenson.—p. 510.
Principles of General Anaesthesia in Childhood. P. Westhead.—p. 514.
Medical Problems of the Aged Sick: Practical Approach to Bed Sores, Incontinence and Restlessness. T. N. Rudd.—p. 521.

Presse Médicale, Paris

59:1381-1412 (Oct. 24) 1951. Partial Index

- Possible Presence of a Demyelinating Process Affecting the Spinal Cord in Acute Anterior Poliomyelitis, and Its Occasional Significance. P. Mollaret, I. Bertrand and H. Mollaret.—p. 1381.
*Combined Use of Chaulmoogra Oil and Streptomycin in Treatment of Pulmonary Tuberculosis. H. Warembourg and G. Niquet.—p. 1387.
*Treatment of Dupuytren's Contracture by Plastic Surgery Using Z-Shaped Incisions Along the Length of the Finger up to the Center of the Palm. M. Iselin and G. D. Dieckmann.—p. 1394.

Chaulmoogra Oil in Pulmonary Tuberculosis.—Combined treatment with chaulmoogra oil and streptomycin or *p*-aminosalicylic acid was given to 20 patients with advanced pulmonary tuberculosis. Administration of chaulmoogra oil was instituted when streptomycin and/or *p*-aminosalicylic acid had been used previously and seemed no longer effective clinically and roentgenologically. Injections of 2 cc. of chaulmoogra oil (the entire product, not just some of its constituents), with 800 units per gram of vitamin A added, were given daily for seven days, and then 5 cc. of the oil were administered daily for 23 days. Of the 20 patients, 14 obtained good results with persistent improvement of the pulmonary lesions revealed by roentgenologic examination and improvement of the general condition, with increased appetite and gain in weight; 2 patients were improved temporarily and 4 were therapeutic failures. In two patients with good results from two months' treatment with chaulmoogra oil, the former resistance of the Koch bacillus (obtained from the patient's sputum) to 50 units of streptomycin in vitro decreased to a sensitivity to 1 unit of streptomycin in vitro. The chaulmoogra oil was well tolerated, with no untoward reactions. Chaulmoogra oil therefore deserves a place in the therapeutic armamentarium of pulmonary tuberculosis.

Plastic Surgery in Dupuytren's Contracture.—A new method of plastic surgery was practiced in 40 patients with Dupuytren's contracture. Z-shaped incisions were extended in a longitudinal line over the entire length of the involved finger up to the center of the palm. The palmar aponeurosis was completely extirpated through these incisions and the finger then was straightened. Each of the small triangular skin flaps resulting from the Z-shaped incisions was transposed with the flap opposite it to relax the tension, and the flaps were held in place with steel wire sutures. These were not removed for at least two weeks, and the hand was placed on a well padded dorsal splint with the fingers slightly flexed. The wounds healed in an average time of 31 days. Good results with complete extension and flexion of fingers were obtained in 24 patients, moderate results with limited extension or limited flexion in 8 patients, and unsatisfactory results in 7, with amputation of the finger required in 5 and recurrence in 2. One patient was not followed. A classification of Dupuytren's contracture in four degrees has been

attempted. The greatest percentage of therapeutic failures or of unsatisfactory results were observed among the patients with involvement of the fifth finger, who also had the highest incidence of fourth degree lesions. Patients with involvement of two or more fingers presented the most difficult technical problems. The results obtained in the authors' cases proved that two-thirds of the patients may obtain recovery with surgical treatment and only from this, while failures in about 15% must be expected.

59:1433-1452 (Nov. 3) 1951

Esterized Fatty Acids in Pathology of Liver. E. Chabrol, M. Böszörményi, P. Fallot and P. Deslypère.—p. 1433.

*Behavior of Heart of Patients with Endocarditis Treated with Antibiotics. P. Broustet.—p. 1434.

Antibiotics in Endocarditis.—Of 23 patients with acute bacterial endocarditis treated with penicillin, 15 had functional disturbances of the cardiac muscle during the febrile stage of the disease or immediately after the temperature returned to normal. Although cardiac decompensation occurs rarely in endocarditis, cardiac dilatation and asystoles may result from valvular destruction or involvement of the myocardium. According to the classic concept, the antibiotics do not exert a favorable influence on cases of endocarditis complicated by cardiac failure; certain investigators even consider this complication irreversible. But there are exceptions. In four of the author's patients, following administration of penicillin, the asystoles disappeared simultaneously with the restoration of the temperature to normal. The functional symptoms subsided as the infection cleared, even in two patients who were not given cardiac tonics. In contrast to these observations, the antibiotics, particularly penicillin, may cause sudden cardiac failure associated with coronary occlusion in patients with endocarditis. It is suggested that these undesirable side-effects may be the result of the allergenic power of certain antibiotics. Thus the response of the heart to the antibiotics varies and each patient presents an individual problem. Therapeutic results may be improved by determining the infectious etiology of the asystoles, early institution of treatment, and use of the antibiotic indicated for the pathogenic agent.

59:1493-1512 (Nov. 14) 1951. Partial Index

*Treatment of Bouillaud's Disease with Cortisone and Corticotropin. F. Coste and M. Oury.—p. 1493.

Part Played by Reflux in Digestive Pathology, Particularly in Pathogenesis of Esophageal Dyskinesia, Esophagitis, Dyspepsia and Gastritis. A. Lambling.—p. 1496.

Cortisone and Corticotropin in Rheumatic Heart Disease.—Of 43 patients with rheumatic heart disease treated with cortisone and corticotropin (ACTH), 25 presented symptoms of severe rheumatic carditis. Of these 25, 4 died from malignant rheumatic heart disease, but only 2 who died had been treated with the hormones for more than three days. Two patients were therapeutic failures, while 19 were improved considerably. Of the remaining 18 patients, 5 had recurrent carditis with rheumatic symptoms that subsided rapidly while the signs of chronic cardiovalvulitis remained unchanged; of 4 patients with recent carditis, 3 made a complete recovery; the hearts of 9 patients with acute articular rheumatism, 5 of whom apparently had endocarditis, appeared normal on clinical, roentgenologic, and electrocardiographic examination at the termination of treatment. Because of the small number of patients with rheumatic heart disease treated with cortisone and corticotropin, definite instructions for treatment cannot be given, but the authors' experience suggests that to check the inflammatory process as rapidly as possible treatment should be started with corticotropin, while later on either corticotropin or cortisone may be employed. At least four daily injections of corticotropin at regular intervals are advisable, while injections of cortisone in microcrystalline suspension may be given every second day. In cases of acute articular rheumatism without carditis or with incipient carditis, treatment should be given for four weeks, while in cases of severe rheumatic heart disease it should be continued for more than two months. The results obtained by the authors suggest that it is possible to control some of the manifestations of rheumatic heart disease with corticotropin or cortisone. The general and functional rheumatic symptoms responded promptly, but,

contrary to Hench, the French workers observed that tachycardia requires two to three weeks to disappear, and they did not observe secondary bradycardia. Erythrocyte sedimentation rates and fibremia responded more slowly than rheumatic symptoms. Pericarditis showed pronounced improvement, as did endocarditis and myocarditis. Although the hormone treatment might not shorten the acute phase of rheumatic heart disease, it seems to control progressive involvement, particularly of the tissues of the heart. Satisfactory results depend on early treatment; cardiac sequelae may be prevented by starting treatment before the occurrence of cardiac involvement or in its initial stage. Oral administration of penicillin seems to aid in the prevention of relapses.

Riv. di Pat. e Clin. della Tuberc., Bologna

24:195-256 (July-Aug.) 1951

Extrapleural Pneumothorax Substituting Inefficient Intrapleural Pneumothorax. G. Zorzoli and A. Valli.—p. 195.

*Simultaneous Bilateral Pneumothorax: Considerations on 340 Cases. N. Sanguigno and A. Vazzana.—p. 200.

Pulmonary Tuberculosis and Congenital Cardiopathy in Unusual Case of Cyanosis. G. Izzo.—p. 215.

*Progressive Tuberculous Polyneuritic Muscular Atrophy. G. Faenzi and A. Mulargia.—p. 238.

Simultaneous Bilateral Pneumothorax.—Simultaneous bilateral pneumothorax was induced in 340 hospitalized patients with pulmonary tuberculosis and was continued for two and one-half years. The second pneumothorax was instituted one to several weeks after the first. The quantity of gas introduced, intrapleural pressure, and frequency of refills depended on the patient's resistance and tolerance. Patients over 50 and those with associated intestinal tuberculosis and heart or kidney disturbances were excluded. Pleurisy, empyema, perforation of the lung, and appearance of new tuberculous foci were the commonest complications. A follow-up five or more years later showed that 94 patients (27.7%) were cured. Pleurisy had occurred in 42 of these patients, and perforation of the lung in 2. Intrapleural pneumolysis or phrenic avulsion had been performed in 15. The condition was stationary in 23 patients, and 27 were not followed. Death occurred in 196 (57.6%). Before pneumothorax the condition of 30 of these patients was critical. In 30 a transient improvement due to the treatment was so great that they were able to resume their work temporarily. Death was due to pleurisy in 84 patients, to perforation of the lung in 15, to hemorrhage in 21, to meningitis in 4, and to toxemia and cardiorespiratory insufficiency in others. The mortality appears high, but there is reason to believe that if simultaneous bilateral pneumothorax had not been performed, the patients would have died sooner and the mortality would have been higher. The treatment was carried out before antibiotic therapy was introduced. With antibiotic drugs to combat complications this treatment may yield better results.

Progressive Tuberculous Polyneuritic Muscular Atrophy.—Pneumothorax was induced in a man, 45, who had pulmonary tuberculosis. Several months later in November, 1949, pain developed in the joints, with high temperature and chills. A year later these symptoms were aggravated by formication, prickling, and sense of cold, first in the lower and then in the upper extremities. Hypotonia was pronounced, and the patient's general condition was poor. Atrophy was observed in the legs and subsequently extended to the thighs, forearms, arms, and later to the feet and hands. Pain and paresthesia increased when the patient was standing. Sudden attacks of muscular hyperesthesia and hyperalgia and marked muscular atrophy in the distal parts of the extremities were the main characteristics of this case. The mode of onset and quick progression of atrophy, the diminution of deep reflexes, the absence of fibrotendinous reflexes, and sensory disturbances justified a diagnosis of tuberculous polyneuritic muscular atrophy caused by tuberculous toxins. This disease entity progresses to death because the toxic stimulus is continuous and causes irreversible degenerative alterations. Antibiotic drugs and massive doses of thiamine (vitamin B₁) were administered to this patient for a long time. His condition was not influenced and is now extremely poor.

Schweizerische medizinische Wochenschrift, Basel

81:1097-1116 (Nov. 10) 1951. Partial Index

Significance of Prolonged Administration of Thiouracil with Respect to Proliferation of Thyroid Tissue. E. Herrmann.—p. 1097.
 Correlation Between Plasma Proteins and Tissue. C. Wunderly and F. Wuhrmann.—p. 1102.
 Effect of Total Heart Extract on Perfusion of Coronary Vessels of Heart by Blood. H. Blömer and G. Schimert.—p. 1108.

Thyroid Proliferation After Prolonged Thiouracil Therapy.—Two patients, a woman aged 54 and a man aged 69, with toxic diffuse goiter were treated with methyl thiouracil for 3 years and 7 years and 10 months, respectively. The total doses of the drug administered were 21.25 gm. and 139.63 gm. Thyroidectomy was performed on both patients. In both microscopic examination of the specimen revealed toxic diffuse parenchymatous hyperplasia with numerous microfollicular and trabecular adenoma anlagen. Adenomas with degeneration into a proliferating struma in the woman and into solid, adenopapillomatous carcinoma in the man were found. In addition a hemangioendothelioma was observed in the latter patient. Rupture of numerous vessels, perforation of the capsule, and infiltrative growth were present in both instances. Animal experiments performed by American and British investigators showed that the time factor plays a considerable part in the production of adenomas and malignant tumors observed in rats that had been treated with thiouracil or its derivatives for 6 to 20 months. The author agrees with the concept of these investigators that the occurrence of adenoma and occasionally of carcinoma, though not caused directly by thiouracil, may be the effect of increased secretion of thyrotropic hormone due to deficient formation of thyroxine, may possibly be the effect of iodine deficiency. Thiouracil and its derivatives should not be considered carcinogenic, but capable of producing thyroid adenomas with possible secondary malignant degeneration. The author therefore cautions against a long continued administration of thiouracil. He advocates surgical treatment of patients with recurrence after a remission had been obtained with thiouracil or its derivatives.

Revue des Hôpitaux de Paris

27:3333-3370 (Nov. 14) 1951

Treatment of Hypertension by Interrupted Prolonged Sleep. G. B. Feldman.—p. 3333.
 Steroid Hormones and Inflammatory Reaction. A. Lichtwitz, S. de Sèze, G. Thiéry and others.—p. 3337.
 Viruses of Seasonal Encephalitis and Their Tropical Origin. P. Lépine.—p. 3354.

Treatment of Hypertension by Prolonged Sleep.—On the basis of Pavlov's concept of the internal inhibition of conditioned reflexes by sleep, the author treated 46 patients with neurogenic hypertension by interrupted prolonged sleep. The 39 women and 7 men between 21 and 55 who were studied were hospitalized for about 30 days. For the first 10 days the patients rested in bed and were subjected to various examinations including oscilometry, measuring of venous pressure and circulatory velocity, ophthalmoscopy, electrocardiograms, and examination of the fundus of the eyes. Ophthalmodynamometric measurements and photographs of the fundus of the eyes were taken in 11 patients. Laboratory examinations included determinations of blood cholesterol, nonprotein nitrogen, alkali reserve, exploration of the excretory function of the liver, function of the kidneys, and basal metabolic rate. On the 11th day treatment by sleep was instituted. Sleep was induced by the administration of amobarbital sodium, which was preferred to phenobarbital because it was readily eliminated. The doses used for the treatment of the first five patients proved to be too high; the doses employed in the remaining 41 patients were 0.3 gm. given twice daily by the oral route or 0.2 gm. given orally in the morning and in the evening for 10 days. The total dose of the drug varied from 4.5 gm. to 6.5 gm. On the fourth or fifth day of the treatment, when the narcotic effect of the drug was diminishing, 0.25 gm. of minopyrine was given twice a day. The synergistic effect of the two drugs was observed frequently. Following the administration of the drug in the morning the patients slept for three and a half to four hours. While still somnolent they were given

a tablespoonful of Bechterew's mixture, and after that they slept again for three and a half to four hours. They then ate their dinner, received the second dose of the drug, and slept through the entire night. Thus an average of 18 hours sleep was obtained in the course of 24 hours. Complications in the central nervous system or other organs did not occur. Satisfactory results with drop of the arterial pressure, disappearance of irritability and anxiety, and restoration of full working capacity were obtained in 28 patients. Fairly good results were obtained in additional 9 patients, while the remaining 9 were therapeutic failures.

South African Medical Journal, Cape Town

25:773-788 (Oct. 27) 1951. Partial Index

*Fat Necrosis of Breast. I. Opeskin.—p. 778.
 Sickle Cell Anaemia: Report of Case with Note on Therapy. I. J. Grek and M. Findlay.—p. 780.
 Late Successful Arterial Embolectomy. H. Katz.—p. 784.

Fat Necrosis of Breast.—Fat necrosis of the breast may resemble the clinical signs of carcinoma very closely, as indicated in 45 cases, in 12 of which a radical mastectomy was performed. Even in early fat necrosis there may be central liquefaction with production of yellowish, oily fluid. Very soon the area appears chalky and is invaded by fibrous tissue that splits it up into rounded and irregular fragments. The lesion feels firm, but it never has the hardness of scirrhous carcinoma. Sometimes the lesion is slightly pigmented by hemosiderin. The tumor may be differentiated from carcinoma by absence of the characteristic yellow spots of epithelial debris and infiltration in surrounding tissues, although there is some adherence. After discussing the microscopic appearance of the lesion, the author describes the history of a patient in whom fat necrosis of the breast was at first diagnosed as inoperable scirrhous carcinoma, but the following factors suggested the advisability of a biopsy before treatment: the history of such a large hard mass was short; the affected nipple was lower than normal and not retracted; the pigmented area around the areola was not typical of carcinoma; and the axillary glands were small and not hard. The author stresses that rapid increase in the size of a hard mass in a breast should suggest the possibility of fat necrosis, especially when associated with a history of trauma. The macroscopic appearance of fat necrosis is typical and in doubtful cases the mass should be incised before radical mastectomy is done.

Ugeskrift for Laeger, Copenhagen

113:1397-1426 (Oct. 18) 1951. Partial Index

*Fetal Toxoplasmosis. V. A. Jensen.—p. 1397.
 Problems in Verification of Foot-and-Mouth Disease in Man. E. Michelsen.—p. 1401.
 Streptomycin Treatment of Acute Tuberculous Otitis Media. P. M. Christensen.—p. 1406.
 After Administration of Dihydrostreptomycin: Case. J. Guldberg-Møller.—p. 1409.
 Kveim's Reaction Applied in Diagnosis of Benign Lymphogranulomatosis (Schaumann). G. Spøndergaard.—p. 1412.

Fetal Toxoplasmosis.—Jensen says that toxoplasmosis in adults is usually latent and is manifested by development of specific antibodies in the blood or by the fact that children with manifest toxoplasmosis are born to infected mothers. The cardinal symptoms in congenital toxoplasmosis are bilateral chorioretinitis, internal hydrocephalus, intracerebral calcifications, and convulsions. Toxoplasma are transmitted from mother to child in the uterus. Three infants with hydrocephalus and one infant with dyssynostosis cranii, all found to have toxoplasmosis, were admitted in the neurosurgical department of Aarhus Kommunehospital during the last two years. The results of histological examination of the retina in the three fatal cases are described in detail. One infant was a twin; his twin sister is well and has a normal fundus. One of the mothers later gave birth to a healthy child. Tissues in the differentiation stage are more susceptible to intrauterine injury by virus than other tissues, which is the reason that the retina and chorioidea in the macula region, where differentiation of tissue occurs late, are oftenest the place of least resistance to toxoplasma.

BOOK REVIEWS

The Electrical Activity of the Nervous System: A Textbook for Students. By Mary A. B. Brazier, B.Sc., Ph.D. Cloth. \$5. Pp. 220, with 96 illustrations. The Macmillan Company, 60 Fifth Ave., New York 11, 1951.

This book summarizes for students of neurophysiology the facts thus far gathered relating to the electrical excitation of nerves, the nature of the nerve impulse, and the electrical phenomena observed in nerve fibers and in masses of nervous tissue. It is not intended to be a technical manual and presupposes a considerable knowledge of anatomy, as well as experience in the laboratory, on the part of the student. Nevertheless, the author's fortunate style lends a certain vividness to the presentation. This will be appreciated by those who recall the oppressive dullness of some comparable works written in the past. The wealth of new information presented is gratifying, and the reader cannot help imagining the pleasure that Galvani, Helmholtz, and Du Bois-Reymond would take in the recent developments in their field of research. Special praise is merited by the concluding chapters on the electrical activity of the eye, ear, other sense organs, and the brain, with the judicious treatment of the subject of normal and abnormal electroencephalograms. It is unlikely that every student will understand the allusion to the automatic electronic analyzer (page 198) or be aware of the pitfalls of harmonic analysis, but an excellent bibliography at the end of each chapter gives clues to unanswered questions. There is also a commendable index. This book should be available in every library devoted to the basic medical sciences.

Bacterial Toxins. By W. E. van Heyningen, M.A., M.Sc., Ph.D., Senior Research Officer, Sir William Dunn School of Pathology, University of Oxford. Cloth. \$3.50. Pp. 133, with 12 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford; Ryerson Press, 299 Queen St., W., Toronto 2B, 1950.

This monograph was written because the subject of bacterial toxins has been neglected in most textbooks. Discussions of toxins of the gram-positive bacteria occupy most of the text; these include toxins of the clostridia, the corynebacteria, the streptococci, and the staphylococci. The toxins of these organisms are generally more toxic than those of the gram-negative group, and they are capable of being neutralized and toxoids can be formed from them. The gram-negative group includes *Shigella dysenteriae*, *Brucella*, *melitensis*, *Vibrio cholerae*, the neisseriace, *hemophilus pertussis*, *Pasteurella pestis*, the *Rickettsia*, and the viruses. Most of these are endotoxins about which less is known. References to more than 400 published articles are given. The book is recommended to anyone interested in this subject.

Amenorrhea. By Lawrence M. Randall, M.D., and Thomas W. McElin, M.D. Publication number 109, American Lecture Series, monograph in American Lectures in Endocrinology. Edited by Willard O. Thompson, M.D., Clinical Professor of Medicine, University of Illinois College of Medicine, Chicago. Cloth. \$2.25. Pp. 74. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, 1951.

This is a short monograph on the classification, investigation, and treatment of amenorrhea of primary and secondary origin. Unfortunately, some confusion is caused by the citation of many authorities without an attempt to organize or draw conclusions from their material. However, this criticism, if it can be called that, does not extend to the excellent review of the Russian investigations and the section on therapy. In the latter, the roles of the estrogens, thyroid, gonadotropins, progesterone, and combined hormonal therapy are briefly reviewed by abstracts of the literature. Less frequently utilized forms of therapy, such as roentgen ray techniques and neostigmine, are also included.

A Textbook of General Physiology. By Hugh Davson, D.Sc., Scientific Staff, Medical Research Council, London. Cloth. \$7. Pp. 659, with 1012 illustrations. Blackiston Company (division of Doubleday & Company, Inc. 1012 Walnut St., Philadelphia 5; J. & A. Churchill, Ltd., 104 Gloucester Pl., Portman Sq., London, W.1, 1951).

The author has collected in this book the results of modern research of the general physiologist, who "attempts to explain living phenomena in terms of concepts familiar in the basic sciences of physics and chemistry." The book has six major visions: the structural basis of living matter, the transformation of energy in living systems, the transport of water and solutes, the characteristics of excitable tissue, the mechanism of muscle contraction, and the emission and effects of light. The intention of the author was to produce a work comparable to the classic "Principles of General Physiology" of William Bayliss. In this he has largely succeeded, for he has caught the spirit of his predecessor admirably. Though Bayliss may never have been concerned with semantics and operational analysis, he had the good sense to avoid defining a given word in terms of other indefinable words. He illustrated general principles by means of specific instances and he recognized the need of describing apparatus and procedure before stating results and conclusions. These features also characterize the present volume, and the present author has had the advantage that many of the things that could be pictured only mentally by Bayliss can now be seen and measured by modern methods as roentgen ray diffraction, electron microscopy, phase microscopy, ultrafiltration, ultracentrifugation, electrophoresis, and the use of radioactive isotopes. Furthermore, the limitations of living systems by arrangements of cells and condensers have undergone unexpected development.

The author expresses his regret at the omission of a number of subjects; to his list might be added the production, effect, and perception of sonic and ultrasonic vibrations. It is to be hoped that such material will be supplied in a future edition. The present edition deserves high praise for clarity of exposition, beauty of illustrations, helpful bibliographies, and good index.

Experimental Physiology for Medical Students. By D. T. Harris, D.Sc., F.Inst.P., H. P. Gilding, M.A., M.D., Professor of Physiology, University of Birmingham, and W. A. M. Smart, B.Sc., M.B., B.S. edition. Cloth. 21s. Pp. 305, with 267 illustrations. J. & A. Churchill, 104 Gloucester Place, Portman Sq., London W.1, 1951.

The first section of this excellent book is devoted to experiments in physiology and the second to experiments in pharmacology. Both sections afford illustrations of the handicaps under which these two subjects must be taught in England because of the lingering influence of antivivisectionists. It is gratifying, nevertheless, to find the metric system used throughout; in other respects, too, the book is abreast of the times.

Commendable are the figures, which include a sufficient number of wiring diagrams to stimulate the student's interest in audiometers and similar appurtenances of modern physiological medicine. The section on special senses contains many good experiments. The experiments on taste (page 266) could be enriched by the inclusion of phenylthiourea, which not only impresses the student with the importance of individual differences but is of historic interest because of the developments that have followed its discovery. The subject of basal metabolism could be freed of a source of much confusion and error by eliminating the surface area concept, following the recommendation of Dreyer. In connection with sphygmomanometry (page 11) it might be well to reproduce the carefully prepared recommendations of the Committee of the American Heart Association for the Revision of Standardization of Blood Pressure Readings. The various methods of sphygmomanometry are also an excellent source of data for the calculation of reliability indexes and for exercises in practical biometry. At this and several other points in the book the authors might well introduce some of the simple concepts of statistical methodology, particularly that of contrast or "control" and the fourfold table. In the pharmacology

ology section it must be noted that the statement "Broncho-instructors . . . are only of pharmacological interest" (page 289) is no longer true, since the development of "nerve uses" as a threat in warfare and of organic insecticides in agriculture, and that Tyrode's solution (pages 276 and 299) ought to be replaced by stabler media, such as the Sollmann-Rademaekers solution.

The book is attractive in appearance, the printing is remarkably free from errors, and there is a good index. It is to be recommended to physiologists as a rich source of inspiration and practical suggestions.

Biological Effects of External Beta Radiation. Edited by Raymond E. Rikle, Professor of Radiobiology, Institute of Radiobiology and Biophysics, University of Chicago, Chicago. National Nuclear Energy Series: Manhattan Project Technical Section. Division IV: Plutonium Project. Second, Volume 22 E. Cloth. \$3.25. Pp. 242, with illustrations. McGraw-Hill Book Company, Inc., 330 W. 42d St., New York 18; Aldwych House, Aldwych, London, W.C.2, 1951.

This volume records some of the results of research done under the Manhattan Project and the Atomic Energy Commission between 1942 and 1945. It has eight contributing authors and 16 chapters. The greater part of the results reported were obtained by Dr. I. R. Raper while at the Clinton Laboratories during World War II.

The chapters entitled "Techniques of External Irradiation with X-Rays" records the methods used by the group at the Clinton Laboratories for preparing and evaluating the radioactive sources. Although some work under the Manhattan Project was done with radioactive strontium (Sr^{90}) and radioactive yttrium (Y^{91}), the lack of suitable intense sources of these isotopes prevented their use in the biological experiments; consequently, these experiments were limited to the use of radioactive phosphorus (P^{32}). The balance of the book records the effects on various laboratory animals of beta irradiation as compared with gamma irradiation, showing gross and microscopic effects of restricted and total surface irradiation, additive effects, delayed effects, and recovery rates, blood changes and metabolic derangements. The tumor inducing action of superficial radiation is discussed in a separate chapter. The rapidly increasing application of artificial radioactive isotopes to medical problems makes it of volume of great value to those already using these agents and to those contemplating their use.

Journey Together. By Turnley Walker. Cloth. \$2.50. Pp. 144. David McKay Company, Inc., 225 Park Ave., New York 17, 1951.

This is a fascinating and well-written autobiography telling the story of one man's rehabilitation after he was handicapped by the residual paralysis of poliomyelitis. The reader's interest is gathered momentum as he follows the story of the author's finding himself as a person again and his return to the world outside the protective security of the hospital. This book provides a glimpse of the universal despair, as well as the gratifying feeling that follows mastery over handicap, felt by all those utterly stricken with a disabling disease. It could well be used as a source of encouragement by many of the handicapped in thinking about a psychological adjustment to their disability, and could provide them with determination to develop their remaining faculties to a point where they can again lead happy and useful lives.

Caring for the Premature Baby. By Lillian Saltzman. Cloth. \$2.50. Pp. 2, with illustrations. Chapman & Grimes, Publishers, 30 Winchester St., Boston 16, 1951.

This is an excellent book, directed to the layman, concerning the minute technicalities of care of the premature infant. It would prove helpful to those in communities in which home births are prevalent and hospital care for premature infants is not available, and should be of value to both practical and trained nurses. The book covers general facts concerning the anatomy and physiology of the premature infant and its early care and gives specific details concerning infection, cyanosis, clothing, bathing, and feeding. The problem of humidity does not receive sufficient stress; it is now generally recognized that

adequate humidity is essential for the premature infant. Also, the oxygen concentration recommended by the author for these infants seems too high. Informative discussions of the various types of incubators and of diarrhea and intestinal disorders are included. Persons entrusted with the care of a premature infant should find this book of assistance.

Leibesübungen mit Körperbeschädigten: Ein Lehr- und Arbeitsbuch für Körperbehinderte und ihre Betreuer. Von Hans Lorenzen. Neue Folge Heft 45, Arbeit und Gesundheit; Sozialmedizinische Schriftenreihe aus dem Gebiete des Bundesministeriums für Arbeit. Herausgegeben von Professor Dr. phil. et med. M. Bauer und Dr. med. F. Paetold. Paper. 7.50 marks. Pp. 218, with 182 illustrations. Georg Thieme, Diemershaldenstrasse 47, (14a) Stuttgart O; agents for U. S. A., Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1951.

This is an interesting monograph on the subject of exercises for persons with bodily handicaps. Coming out of Germany, the traditional bulwark of formalism in physical education and in sports, this book shows a remarkable advance in the concept of making physical education a source of pleasure in the actual doing, as well as a means toward an objective, such as body building, and, in the case of the handicapped, rehabilitation. The book deals with organizations and methods, with general body development, with the medicine ball and the usefulness of tumbling, swimming, diving, and lifesaving, and with many variations of competitive sports for arm and leg amputees and others with various forms of body deformities. It is concerned particularly with war casualties but is equally applicable to those handicapped from any other cause. Allowing for the fact that, despite its progress toward informality, it still contains considerable evidence of characteristic German formalism, this book contains valuable suggestions for physicians or physical educators dealing with exercise for the handicapped. The illustrations are numerous and clear, and they help to overcome language difficulties for those who do not read German fluently.

Comparative Physiology of the Thyroid and Parathyroid Glands. By Walter Fleischmann, M.D., Ph.D., Instructor in Pediatrics, Johns Hopkins University School of Medicine, Baltimore. Publication number 118, American Lecture Series, monograph in American Lectures in Endocrinology. Edited by Willard O. Thompson, M.D., Clinical Professor of Medicine, University of Illinois College of Medicine, Chicago. Cloth, \$2.25. Pp. 78. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, 1951.

This monograph contains a review of literature dealing with the comparative physiology of the thyroid and parathyroid glands. The author, who has himself contributed widely to this field, has covered the subject adequately, describing pertinent discoveries in organisms ranging from ammocoetes to man. The hormones subserve such basic functions in the animal economy that it is not surprising to learn they are identical throughout the vertebrate phylum. A study of comparative endocrinology is thus not without value in understanding hormonal functions in the human. The author has included a bibliography of over 100 references. Although the monograph is of value primarily to the experimental endocrinologist, the internist will find it of some interest. The format and style are good; a more extensive treatment of the subject and inclusion of illustrations would have been desirable.

The Curriculum in Health and Physical Education. By Leslie W. Irwin, Ph.D., Professor of Health and Physical Education, School of Education, Boston University, Boston. Second edition. Cloth. \$4. Pp. 382. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1951.

This book covers the curriculum in physical education in some detail and school health and safety in a more general way. A discussion of the place of physical education in modern living and education is followed by a rather specific outline of activities for the various grade levels. Descriptions of intramural, inter-school, and informal sports programs suitable for the various age groups are also presented, with emphasis placed on the need for the type of organization and administration that will permit desirable health and educational outcomes. A strong plea is made for careful consideration of individual differences pupils in the planning of the physical education c

QUERIES AND MINOR NOTES

TREATMENT OF NEPHROSIS

TO THE EDITOR:—In a 52-year-old woman, edema of the ankles and legs developed, without facial edema, nine weeks ago. She vomited twice in the morning. Urine examination showed albumin 4+, with 10 white blood cells, 3 to 4 red blood cells, and no casts. Blood pressure and optic fundi were normal. The red blood cell count was 4,800,000; hemoglobin was 95%; and the white blood cell count was 10,050, with 53% neutrophils and 40% lymphocytes. Blood chemistry showed normal blood urea nitrogen but a total protein of 4.7 gm. per 100 cc., with an albumin-globulin ratio of 1.6 to 1. Results of the Fishberg concentration test were normal. The temperature never exceeded 99.8 F. The heart and lungs were normal, as were an electrocardiogram and chest roentgenogram taken a year ago. During the following weeks, the patient was put on bed rest, and given a salt-poor and fat-poor diet, vitamin B capsules, liver extract, protein hydrolysate, and ammonium chloride. There was no change in the urinary findings, except for the appearance of hyaline casts. The daily total urinary albumin was between 6 and 11 gm. The total blood protein went down to 3.01 gm. per 100 cc., but the albumin-globulin remained above 1. The sedimentation rate was between 40 and 30 mm. per hour. Total cholesterol was 750 mg. per 100 cc., with the cholesterol esters about 65 to 69% of the total. Liver function tests were normal. Hematocrit was 46%.

The edema could be checked moderately by the administration of ammonium chloride and occasional injections of 1 cc. of mercaptopimerin (thiomerein[®]) sodium; however, the effect was only temporary. A urine culture was done, but no growth was found. For a few days, gantrisin[®] (3-4-dimethyl-5-sulfanilamido-isoxazole) was given, with no effect, and, because the urine excretion diminished, it was discontinued. I had to stop the administration of liver extract and protein hydrolysates because the patient completely lost her appetite and felt nauseated. After discontinuation of these medications, the general condition improved. The urinary findings, together with the hypoproteinemia, the normal blood pressure, and the normal fundi warrant the diagnosis of chronic nephrosis. What other therapy is advised? What is the prognosis?

Frederick D. Regensberg, M.D., Butler, Pa.

ANSWER.—Aside from the large number of red blood cells in the urinary sediment, the case described could be an example of pure lipid nephrosis occurring late in life; the red cells suggest that this may be nephrosis occurring in the subacute stage of hemorrhagic glomerulonephritis. An antistreptolysin titer, done soon after onset, may be useful in confirming the latter diagnosis, as would careful studies of the sediment for red cell casts. In pure lipid nephrosis, and, less often, in nephrotic stages of glomerulonephritis, the disease has been favorably altered by the use of nitrogen mustard, cortisone, or corticotropin. Spontaneous remission may occur after intercurrent viral infections. Diuresis, with no effect on the course of the disease, can be produced by administering 50 gm. of human albumin daily. High protein diets and hydrolyzed protein infusions have no favorable effects, but, as with albumin infusions, they actually increase proteinuria. Low fat diets and thyroid extract rarely alter the plasma lipid levels, which return to normal after proteinuria ceases. As the condition may last for months or years, bed rest is not advisable, but avoidance of fatigue and chilling is essential. Use of sulfonamides and antibiotics is futile, except for intercurrent infections. Dietary sodium restriction and mercurial diuretics, together with ammonium chloride and cationic exchange resins, are helpful in controlling edema.

The administration of 200 mg. of cortisone daily, in four oral doses, for 3 days and then 100 mg. a day for 10 days, with abrupt cessation of therapy, should be tried first. Remission may occur after the drug has been discontinued. Acetylsalicylic acid, in doses of 4 gm. daily, may markedly reduce proteinuria, but few remissions have resulted from the use of this agent. The life prognosis is usually good in older patients with nephrosis or those with subacute nephritis with normal blood urea. Recovery is rare in the latter, but it may occur spontaneously in about half of the former group.

LATE SEQUELAE OF DEEP ILIOFEMORAL THROMBOSIS

TO THE EDITOR:—Twenty years ago a woman had a "milk leg" and pulmonary embolism following a delivery. Today both lower limbs are swollen, the left more than the right, and there are some superficial varices. She has been wearing elastic stockings for years, apparently without discomfort. I believe that she has deep thrombosis. It has also been my impression that patients with deep involvement cannot stand an elastic stocking; however, in this patient there can be no question of the deep involvement. The patient has been advised to have an operation. Is it not contrary to all reason and orthodox teaching that superficial varices should not be obliterated if there is a deep thrombosis? If the superficial femoral were ligated would the subcutaneous veins be able to carry on the circulation? My patient has unfortunately had some of the superficial veins obliterated by injection.

M.D., Pennsylvania.

ANSWER.—The decision as to whether the late sequelae of deep, iliofemoral thrombosis are to be treated with well-fitting elastic hose from toes to groin, with ligation and stripping of the superficial varicosities, or with division of the deep venous system, cannot be made without a study of the nature of the venous insufficiency that remains after a thrombotic occlusion of the deep venous system. Many patients are comfortable with the elastic hose, show little swelling, and are only discomfited by attacks of phlebitis in the collateral veins, or by supramalleolar indurations, which may ulcerate on slight injury. In more than half of the patients who have suffered an iliofemoral venous thrombosis chronic recurrent ulcerations develop after 20 years. But, if the calves are soft, if the swelling is moderate, and if rapid muscle contractions of the calf by standing on the toes 10 to 15 times visibly empty distended superficial veins, a fair state of compensation exists, and no surgical therapy needs to be considered.

In other patients the superficial, communicating, and deep valves are incompetent, and a marked reflux of blood occurs from above when the patient is upright. Such a patient has an increased venous pressure in the lower extremities when standing. The usual Trendelenburg test gives an idea of how much of this reflux occurs through saphenous and communicating valves. The state of the deep valvular system can be studied by exercising the leg with a tourniquet placed just below the knee. If the superficial veins collapse on exercise and stay collapsed, the deep veins are patent and competent; if the veins collapse and refill after the exercise, the deep venous system is incompetent; if the veins do not collapse on exercise but distend even more, the deep venous system is obstructed. Only after demonstration of the deep valvular incompetence can one consider a ligation of the deep veins, but this clinical test should be corroborated with a suitable venogram. Not more than 10% of all patients suffering from post-thrombotic sequelae will satisfy these criteria; nor will postphlebotic lymphedema improve. The level of deep venous interruption is more effective at a popliteal, than at a superficial, femoral level. (See de Takats, G., and Graupner, G. W.: Division of the Popliteal Vein in Deep Venous Insufficiency of the Lower Extremities, *Surgery* 29:342 [March] 1951.)

CONGENITAL DEFECTS

TO THE EDITOR:—A woman was delivered at term in 1947, at the age of 25, of a normal female child. The second child, a male, was delivered in 1949. At three weeks the infant presented hoarseness, weakness and intermittent cyanosis with no physical findings. Chest x-ray showed a massively enlarged thymus. He received three x-ray treatments at weekly intervals and seemed to improve. He died suddenly two days after the third treatment. Autopsy revealed the enlarged thymus, atelectasis of the upper lung lobes, and a patent foramen ovale. The third pregnancy began as a threatened abortion in November, 1950, but was carried with progesterone and limitation of activity. Several days past the expected date of confinement, delivery was medically induced, since life had not been felt for 24 hours. The patient was delivered of a stillborn male, externally normal. The mother is Rh positive. Autopsy was refused, and the only explanation I could give was the possibility of another organic congenital anomaly. The parents now want to know the probabilities of future congenital anomalies and whether pregnancy should be risked again.

Fred H. McClain Jr., M.D., Mount Union, Pa.

ANSWER.—There is no apparent special reason to fear an abnormal fetus in this patient. Her first baby was normal. Her second baby had no gross defect. The thymus is considered by many to be enlarged normally at birth and requires no treatment. The foramen ovale is often open anatomically but not functionally. The cause of death probably was the atelectasis. The third baby could have died from almost any cause, since autopsy was not done, but there is no reason to suspect a congenital defect. A mother with one congenitally defective baby is no more likely to have a repetition than is the average patient. A mother with two defective babies is more likely to have a repetition. A woman with three defective babies is likely to have defective babies rather consistently.

DERMATITIS FROM DIESEL OIL

TO THE EDITOR:—A railway opened a diesel shop in Chattanooga, and, since its beginning, three years ago, I have had several patients with allergic dermatitis, which appears to be due to contact with diesel oil. I wonder if this condition is commonly noted in similar shops. If so, is there any successful treatment, or possible prevention, by the use of a film to cover the skin?

Cecil E. Newell, M.D., Chattanooga, Tenn.

ANSWER.—Dermatitis from diesel oil is oftener of the contact variety than of the allergic type. Sensitization is possible, but it is unlikely that it would be due to the oil per se; it is probably due to the aberrant proteins of the skin resulting from the contact damage. Also, after contact injury the skin may respond more readily to the allergenic qualities of soaps and other offenders. Diesel oil is a crude petroleum fraction similar to fuel oil, and, thus, is not outstanding as an allergen. The common severe injuries from diesel oil and diesel motors are from flesh penetration from high pressure jet streams received when the oil is thrust into the combustion chambers. This deeply imbedded oil provides traumatic injury and not essentially a dermatitis. The practice of cleaning the skin with this oil is indefensible and should be condemned. Some protection is afforded by hand coatings. Ordinary protective ointments and lotions are of dubious value.

VITAMIN A AND DEAFNESS

TO THE EDITOR:—In the September issue of *Coronet* magazine is an article entitled "Five New Cures for Deafness," by Madelyn Wood. One of these cures mentions the use of large doses of vitamin A. I would like to have an authoritative opinion regarding the use of such doses of vitamin A.

M.D., Tennessee.

ANSWER.—There exists very little scientific evidence for the claim that large doses of vitamin A are beneficial in cases of deafness. Until there have been further published reports of carefully controlled series of cases, this treatment must be regarded as experimental and not of accepted value.

EXPOSURE TO AZOBENZENE VAPOR AND TOBACCO SMOKE

TO THE EDITOR:—A 58-year-old man has worked in a greenhouse for about 10 years, using a compound containing azobenzene and nicotine for fumigation purposes. This is applied by heating the substance, which causes an orange-colored vapor to appear throughout the greenhouse, which is allowed to remain for a period of hours, at the end of which the employee puts on a gas mask and opens all the windows. Except for acute conjunctivitis from contact of the eye with insecticide, he had been in reasonably good health until six weeks ago, when he became acutely ill, with extreme weakness, chills, and a temperature of 104 to 105 F. He was treated with penicillin on the second day of his illness, which was undiagnosed; after this severe soreness and inflammation of the throat, with considerable blindness, developed. This later condition is considered to be acute superficial punctate keratitis of both eyes. Now, six weeks after the original onset, the throat has almost cleared and the eye condition is improving slowly. The patient has had no contact with the azobenzene and nicotine compounds since the beginning of the illness. I would like information on poisoning by azobenzene and nicotine.

M.D., Illinois.

ANSWER.—The fumigator used by the patient appears to be similar to a pressure fumigator described by Blauvelt (New Azobenzene Fumigants, New York State Flower Growers Bull. No. 19, 1947, p. 9.) This device releases clouds of azobenzene vapor and tobacco smoke from a special container holding a mixture of powdered tobacco, potassium nitrate, and azobenzene and which is ignited by means of a "sparkler." The toxic properties of azobenzene are poorly understood, and there is little published clinical data on this compound. By contrast, the injurious effects of nicotine are well known. The acute conjunctivitis may have been caused by exposure to the tobacco smoke, since nicotine and other constituents of the smoke are fairly strong irritants. In addition to conjunctivitis, nicotine may also cause scotoma, narrowing of the field of vision, and diminution of the sharpness of sight in the center of the visual field. The subsequent signs of muscular weakness, chills, elevated temperatures, and inflamed throat could also be caused by exposure to tobacco powder or smoke (Stevenson, H. M.: Acute Nicotine Poisoning as Noted in Manufacture and Use of Nicotine Insecticides, *California & West. Med.* 38:92, 1933). Although subnormal temperature is commoner in nicotine poisoning, temperatures up to 104 F have been reported (Deacon, J. N.: Poisoning by Tobacco applied to the Skin, *Brit. M. J.* 2:61, 1926; Price, J. P.: Acute Nicotine Poisoning with Fatal Outcome in a Child, *Am. J. Dis. Child.* 57:102, 1939). The prognosis in nonfatal cases is usually favorable.

HYDROGEN SULFIDE GAS IN INDUSTRIAL PLANT

TO THE EDITOR:—The workers in an industrial plant have been annoyed by the odor of hydrogen sulfide gas emanating from die cutting machines. The source of this gas apparently is a cooling solution made from vegetable oils and water. Since the gas is most noticeable during the summer months and after the machines have been standing idle over the week-end, it is suspected that bacterial action might be the cause. Your advice will be appreciated.

John D. Lynch, M.D., Manitowoc, Wis.

ANSWER.—The situation described is of common occurrence in the metal fabricating industries. Experience indicates that in the usual situation the quantity of hydrogen sulfide gas is not sufficient to create systemic hydrogen sulfide poisoning, even though that gas is toxic. As mentioned, the offensive odors provide the major disturbance. Many cutting compounds contain added sulfur derivatives, and some oils contain sulfur compounds. In either situation, decomposition leading to the liberation of hydrogen sulfide is readily accomplished, and perhaps is brought about through bacterial action, but some chemical disintegration may arise apart from gross bacterial participation. The remedy for this may be found in the more frequent changing of the supply of the cutting oils without prospective reuse. At the time of oil changing, all possible cleansing of tanks, pipes,

and other parts should be done. During hot weather the life-time of some cutting agents does not exceed one week. Available to manufacturers are several disinfectants, including quaternary ammonium compounds, capable of hampering bacterial growth and action. Such compounds do not sterilize oils, but they do reduce the quantity of bacterial growth to a negligible level. Some manufacturers have reached the conclusion that it is better to discard offending compounds at frequent intervals than to resort to chemical disinfection.

LIGATION OF FEMORAL VEIN

TO THE EDITOR:—*What are the indications for ligation of the femoral vein? May the femoral vein be ligated in a patient whose long saphenous vein previously has been ligated and injected?*

J. F. Brennan, M.D., Clarksburg, W. Va.

ANSWER.—Ligation of the superficial femoral vein is indicated as a preventive measure in amputations of the lower extremities or any other operation below the level of the groin that results in prolonged immobilization or impaired muscle action. In the presence of an acute, deep venous thrombosis at the calf or at popliteal level, it is advised by some who do not use anticoagulants. It is certainly advised when anticoagulants cannot be used, as in the presence of bleeding surfaces, or in hemorrhagic blood dyscrasias. In chronic deep venous insufficiency, when the canalized thrombus destroys the valves, its use is highly debatable. Should reflux of the deep veins be demonstrable by tests and by visualization of the deep venous system, the popliteal level is preferable to the femoral level. Common femoral vein ligation results in persistent edema. Previous obliteration of the long saphenous vein does not contraindicate per se a ligation of the superficial femoral vein, but, if the profunda is left unligated, the reflux will establish itself through the patent and incompetent popliteal vein. The technique of these exposures follows the classical methods for ligating the arteries, to which they often adhere.

TREATMENT OF PARKINSONISM

TO THE EDITOR:—*Please discuss the latest treatment for Parkinson's disease.*

William Bayne Allen, M.D., Kansas City, Mo.

ANSWER.—Therapy in Parkinsonism continues to be symptomatic. Relief of symptoms, when obtained, is only partial. New synthetic antispasmodics have proved more effective than the older belladonna preparations. In this country, trihexyphenidyl (artane®) has been the most popular of the antispasmodics. It is the opinion of most authorities that trihexyphenidyl, in doses of 2.5 to 5 mg. three times a day is, at the present time, the most efficacious medication. The addition of diphenhydramine hydrochloride (benadryl®), in doses of 50 mg. three times a day, to the above medication may potentiate the action of the trihexyphenidyl. Toxic symptoms are manifested by unsteadiness, dryness of the mouth, visual blurring, and, occasionally, by mental confusion. For certain patients, the belladonna derivatives continue to be the drugs of choice.

It is not sufficient to give patients with Parkinsonism medicine. Usually, they also demand and need considerable emotional support and some readjustment of their life situation. Proper physical therapy, with heat, massage, and exercise, often proves beneficial.

EXTRASYSTOLES

TO THE EDITOR:—*I note in several standard works of medicine that extrasystoles assume clinical importance when they appear or increase in frequency during the period of deceleration after exertion. This seems contrary to my experience.*

Henry G. Hadley, M.D., Washington, D. C.

ANSWER.—The statement cited is not borne out by the experience of most observers. In general, extrasystoles are more apt to occur when the heart rate is slowed, particularly during the period of slowing that follows exertion or that occurs during rest. They are generally eliminated temporarily by any factor that increases the heart rate, such as exertion and nitrites. For this reason, it is the consensus that extrasystoles attain greater

clinical significance if they occur during tachycardia or when the heart is accelerated by exercise. However, this is not a universal rule, since extrasystoles of functional origin may also be precipitated by exercise. Therefore, the heart rate at which extrasystoles appear is not an infallible criterion to determine clinical significance of extrasystoles.

MAINTENANCE THERAPY AFTER RAPID DIGITALIZATION

TO THE EDITOR:—*I would appreciate an opinion on the following dosage of digitalis leaf, or digitoxin, following the initial use of lanatoside C ("cedilanid") intravenously. There appears to be a difference in procedure with regard to dosage in different institutions. Assuming 8 cc. of lanatoside C given intravenously has proved to be the effective dose, will the immediate continuation of maintenance doses of digitalis leaf or digitoxin maintain adequate digitalis effect? Or, because of its more rapid elimination of lanatoside C from the system, would it be expected that additional doses of digitalis leaf or digitoxin would be necessary before starting the maintenance dosage? The patient weighs between 125 and 175 lb. (56, 79.3 kg.) and is not elderly. The patient has received previous digitalis.*

M.D., California.

ANSWER.—Initial consideration of a few points about digitalis therapy is of prime importance. 1. Many different techniques of digitalis therapy are authoritatively advised and seem to be satisfactory. There is probably no one best method. 2. It is rarely necessary to digitalize any patient rapidly, and, therefore, the problem stated is not as important in current practice as it once was. Disagreeable toxic effects from digitalis are common that it is important to avoid emergency treatment with large doses of digitalis, except when absolutely essential. Strophanthin and ouabain are still satisfactorily used in emergencies in other countries, and in such countries booster doses of digitalis are not routinely used afterward.

It is sufficient in most cases to begin a simple maintenance dose of digitalis leaf, digitoxin, or digoxin orally immediately after the emergency treatment; however, some authorities recommend slightly larger doses of the maintenance drug for a few days before routine chronic treatment. Each case should be considered individually as to whether there is any need for booster doses.

MATTRESS FOR PERSONS WITH NORMAL BACKS

TO THE EDITOR:—*What is the best type of mattress for persons with normal backs? Do you recommend innerspring mattresses? Do you recommend the new foam filling?*

Angela Quilici, M.D., San Carlos, Calif.

ANSWER.—In considering bedding equipment for the normal person, attention must be directed toward both the mattress and the springs. If the springs sag, the mattress placed on it will sag. For proper sleeping posture, the first essential is a good foundation, springs that will not sag. Box springs and other types, if well made, provide this foundation. The mattress used should give firm support, yet have sufficient surface softness to be comfortable. Certain innerspring mattresses have been designed to provide this firm support and surface softness. The foam rubber mattress, with specially constructed springs, and the innerspring mattress, with its set of springs, seem to provide proper bedding equipment for the normal person.

MENSTRUAL MIGRAINE

TO THE EDITOR:—*In the treatment of menstrual migraine, I have had good results from the use of testosterone given 10 mg. before each expected period. Would a dose of 50 mg. of testosterone each month have harmful effects?*

M.D., Tennessee

ANSWER.—The chances that 50 mg. of testosterone propionate administered once monthly would cause virilism or other harmful changes are slight. There is the possibility, however, that this dosage may delay the onset of the menses.

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BRONCHOGENIC CARCINOMA

ITS FREQUENCY, DIAGNOSIS, AND EARLY TREATMENT

*Alton Ochsner, M.D., Paul T. DeCamp, M.D., New Orleans, M. E. DeBakey, M.D., Houston, Texas
and
C. J. Ray, M.D., New Orleans*

The incidence of bronchogenic carcinoma is increasing more rapidly than that of any other cancer. In 1912 Adler,¹ who was able to collect only 374 cases of cancer of the lung, stated, "On one point, however, there is complete consensus of opinion and that is that primary malignant neoplasms of the lung are among the rarest form of disease." Whereas it was an infrequent lesion 40 years ago, it has become one of the most frequent malignant lesions encountered in men. In the 10 years from 1938 to 1948 the number of fatalities from bronchogenic carcinoma in the United States increased 144%, from 6,732 in 1938 to 16,450 in 1948. In this same period of time the total cancer deaths from all types of cancer, increased 31%, from 149,214 in 1938 to 195,594 in 1948. From 1920 to 1948 the death rate from bronchogenic carcinoma per 100,000 population in the United States increased over 10 times, from 1.1 to 11.3 (Fig. 1). According to Doll and Hill,² deaths from cancer of the lung in England increased fifteenfold from 1922 to 1947. There has been considerable controversy concerning the cause of the unprecedented increase in bronchogenic carcinoma. According to Wynder and Graham,³ excessive and prolonged cigarette smoking is an important factor in the genesis of bronchogenic carcinoma. They found that of their 605 male patients with bronchogenic carcinoma, only 2.6% did not smoke or smoked minimally; whereas over 96% had smoked heavily for over 20 years. In the control male general population these figures were 14.6% and 73.7%, respectively. Levin,

Goldstein, and Gerhardt⁴ also found that there were more smokers among cancer patients than noncancer patients and that patients with bronchogenic cancer usually smoked cigarettes. Watson⁵ found in the Memorial Hospital cases that 37% of the patients with lung cancer and 19% without cancer were heavy smokers. Doll and Hill² showed that in a series of patients with cancer of the lung, 11.6% smoked 500,000 cigarettes or more a year; whereas in a noncancer group only 5.6% smoked that many cigarettes. According to these investigators, "About the age of 45, the risk of developing the disease (bronchogenic carcinoma) increases in simple proportion with the amount smoked, and it is approximately 50 times as great among those who smoke 25 or more cigarettes a day as among non-smokers." Schrek and associates⁶ state: "This positive correlation between the incidence of cigarette smoking and the incidence of cancer of the respiratory tract appeared to be both statistically and biologically significant. There is strong circumstantial evidence that cigarette smoking was an etiologic factor in cancer of the respiratory tract." In Iceland, where smoking has only recently become popular, Dungal,⁷ states that among 417 cancers found in 1,939 necropsies there were only 12 cases of primary carcinoma of the lung.

For some time two of us⁸ have been convinced that there is a causal relationship between the increased incidence of bronchogenic carcinoma and the increased use of cigarettes. There is a distinct parallelism between the

From the Department of Surgery, School of Medicine, Tulane University, and the Ochsner Clinic (Drs. Ochsner, DeCamp, and Ray) and the Department of Surgery, College of Medicine, Baylor University (Dr. DeBakey).
Read before the Section on Diseases of the Chest at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 15, 1951.

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sale of cigarettes and the incidence of bronchogenic carcinoma (Fig. 1). The annual production of cigarettes per capita population (including men, women, and children) increased from 46.3 in 1903 to 2,541 in 1948. The latter figure excludes those produced for foreign consumption. Because the carcinogenic effect of cigar-

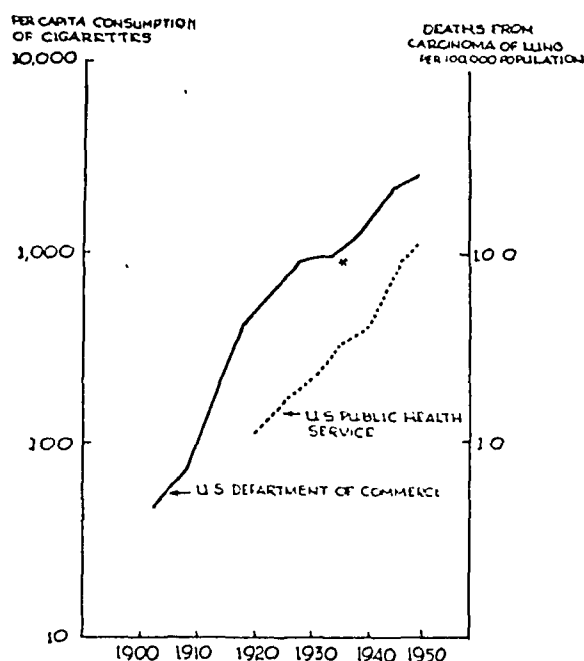


Fig. 1.—Comparison of increasing death rate from bronchogenic carcinoma with the increasing consumption of cigarettes in the United States. * = exported cigarettes deducted in 1933 and subsequently.

ette smoking does not become evident until after many years of smoking (approximately 20), it is frightening to speculate on the possible number of bronchogenic cancers that may develop as the result of the tremendous numbers of cigarettes consumed in the two decades from 1930 to 1950. From 1920 to 1930 the annual number of cigarettes per capita increased from 480 to 930 (approximately 2 times). In the decade 20 years later, i. e., from 1938 to 1948, during which time the carcinogenic effect of the smoking in the earlier decade should have become evident, the number of bronchogenic carcinomas per 100,000 population increased from 4.2 to 11.3. In the 18 years from 1930 to 1948 the annual number of cigarettes per capita consumed increased from 930 to 2,541 (2.6 times), which suggests that if there is a causal relationship between cigarette smoking and bronchogenic carcinoma the deaths per 100,000 population from this cause may be expected to increase from 11.3 to 29.4 by 1970. With the predicted death rate from bronchogenic carcinoma of 29.4 per 100,000 population in 1970, it may be estimated that the annual deaths from this cause will increase from 16,450 in 1948 to 47,000 in 1970. In 1920 deaths from bronchogenic carcinoma represented 1.1% of all cancer deaths; in 1930, 2.2%, and in 1948, 8.3%. It may be predicted that in 1970 18% of all cancer deaths will be due to bronchogenic carcinoma if present trends continue. Because of increased cigarette smoking it is likely and probable that bronchogenic carcinoma soon will become more fre-

quent than any other cancer of the body, unless something is done to prevent its increase. In 1949 over twice as many patients with bronchogenic carcinoma as with gastric cancer were admitted to the Memorial Hospital.

Unfortunately, bronchogenic carcinoma begins so insidiously and because with few exceptions it occurs in persons who smoke excessively and have a cigarette cough, relatively little attention is paid to the early manifestations of the disease. Because of this and also because of the fact that the profession generally is not cognizant of the frequency of bronchogenic carcinoma, there may be considerable delay in diagnosis. Overholt and Schmidt¹⁰ stress the importance of the "silent phase" of bronchogenic carcinoma in which there are few or no symptoms. They report 65 cases, 19 of which were malignant and 39 benign. The resectability rate in the former was 79%. Subsequently, Overholt¹¹ reported 145 cases in which pulmonary shadows were detected on chest surveys, of which 51 were neoplastic and 35 malignant. He states:

If the patient waits for symptoms and if the delays that follow in the average case are added to this time lost, approximately 90% of the lesions have by that time extended to structures outside the lung. The possibility of cure, therefore, is limited to a meager 10% in the symptomatic stage of the disease. To explore and to carry out excisional treatment during the silent phase will set treatment ahead by months or years. In our clinic when prompt treatment has followed discovery of cancer by survey, all lesions have been resectable and 75% have shown no evidence of lymphatic spread.

All patients in the group are still living. In our series of 948 cases of bronchogenic carcinoma, resection was possible in only 332 cases (35%). The average duration of symptoms in the latter group was 12.3 months. Only three patients were asymptomatic; in one the lesion (by x-ray) was 1 cm. in diameter, and in the other two it was 2.5 cm. Nine patients had symptoms less than one month. In one the lesion measured 2.5 cm.; in five, 6 to 8 cm.; and in three, 10 cm. or over. Nineteen patients had symptoms from one to two months. In four the lesion measured 2 to 3.5 cm.; in seven, 5 to 7 cm.;

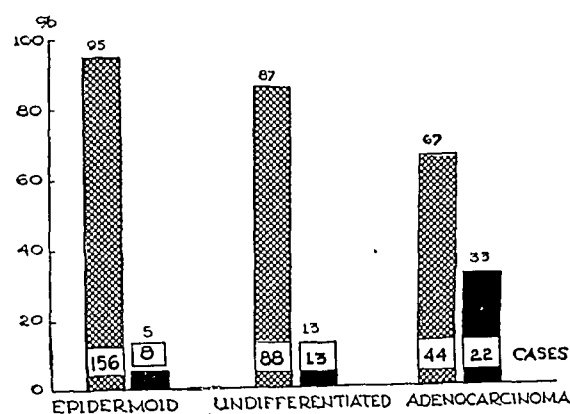


Fig. 2.—Sex incidence by histological types in 331 cases of bronchogenic carcinoma in which resection was done. Hatched bar represents males; black bar, females.

in four, 7.5 to 10 cm.; and in four, over 10 cm. Thus, of 332 cases in which pneumonectomy was done, symptoms for two months or less occurred in only 31. Obviously, any malignant lesion in which there is a delay of over a year has relatively little chance of cure.

The present report is based on a series of 948 patients with bronchogenic carcinoma observed by us in New

9. Deleted in proof.

10. Overholt, R. H., and Schmidt, I. C.: Silent Phase of Cancer of Lung, *J. A. M. A.* 1:11:817 (Nov. 19) 1949.

11. Overholt, R. H.: Cancer Detected in Surveys, *Am. Rev. Tuberc.* 62: 491, 1950.

reans at the Ochsner Clinic and at the Charity Hospital. Because Charity Hospital is an institution to which white and Negro patients are admitted with about equal frequency, it is possible to determine fairly accurately the racial incidence of disease. Bronchogenic carcinoma is more frequent in white men than in Negro men, the

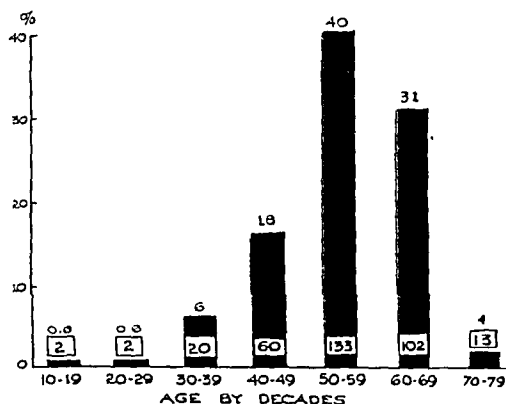


Fig. 3.—Age incidence in 332 cases in which resection was done. Figure white bar indicates number of cases

pective percentages of expected incidence being 118 and 80.

Bronchogenic carcinoma is primarily a disease of men, probably due to the fact that the bronchial mucosa in men is more susceptible to malignant change than in women. It has been suggested that since women are beginning to smoke as much as men the incidence in women will increase. However, it is our belief that whereas there will be some increase in the incidence of bronchogenic carcinoma in women, it will always be more prevalent in men. In the present series of patients, 840 were men and only 108 women. The type of lesion varies in the two sexes (Fig. 2). Ninety-five per cent of the patients with epidermoid carcinoma were men, while only 5% were women. On the other hand, 33% of the patients with adenocarcinoma were women, and 67% were men. Undifferentiated carcinomas occurred predominately in men (87%). Of the 288 men in whom pneumonectomy was done, 54% had epidermoid carcinoma, 1% undifferentiated carcinoma, and only 15% adenocarcinoma. Of the 43 women, only 19% had epidermoid carcinoma, 30% had undifferentiated carcinoma, and 51% had adenocarcinoma.

Bronchogenic carcinoma, as other types of carcinoma, is primarily a disease of older persons, the greatest incidence being in the fifth, sixth, and seventh decades (18%, 40%, and 31%, respectively) (Fig. 3).

PATHOLOGY

Primary carcinoma of the bronchus can occur in any part of the bronchial tree (Fig. 4). Over half in our series occurred in the upper lobes. This is of significance, since lesions of the upper lobe bronchi are less likely to be visible on bronchoscopic examination because they are located "around the corner." The two sides were involved with about equal frequency the right 53%, the left 47%. Whereas previously it was thought that primary carcinoma of the bronchus occurred frequently in the main stem bronchus, this contention is not substantiated in our series. Only 13 of the primary carci-

nomas in the cases in which resection was done were in the main stem bronchus, 188 were in a lobe bronchus, and 123 in the periphery. Of 331 cases in which resection was done, 49.5% of the carcinomas were epidermoid, 30.5% were undifferentiated, and 19.9% were adenocarcinomas. Epidermoid carcinomas were infrequent in women, but adenocarcinomas occurred relatively more frequently in women than in men. Of the 165 epidermoid carcinomas, 4% were in the main stem bronchus, 66% in a lobar bronchus, and 30% in the periphery. Of the 95 undifferentiated carcinomas, 3% were in the main stem bronchus, 54% in a lobar bronchus, and 43% in the periphery. Of the 64 adenocarcinomas, 5% were in the main stem bronchus, 44% in a lobar bronchus, and 51% in the periphery. It is thus seen that, although lobar bronchi are involved more frequently than any other bronchi, adenocarcinomas occur more frequently in the periphery. The relative incidence of adenocarcinoma decreases with advancing age; whereas the incidence of epidermoid carcinoma increases with advancing age. The latter is probably due to the carcinogenic effect of tobacco acting for a longer time. According to Wynder and Graham,¹² "Over 96% of patients with cancer of the lung have smoked for more than 20 years and over 80% have smoked for more than 30 years." Adenocarcinomas probably originate in embryonic rests, as suggested by Graham¹² who states, "Those carcinomas designated as adenocarcinoma, oat cell, and round cell carcinoma arise from an embryonic bronchial bud which has failed to develop into normal tissue and has remained dormant for many years before being transformed into a carcinoma." Because they originate in congenital rests they are likely to become evident at earlier ages. Their incidence is not affected by smoking.

CLINICAL PICTURE

As mentioned previously, the clinical manifestations of bronchogenic carcinoma begin insidiously and are likely to be disregarded both by the patient and his

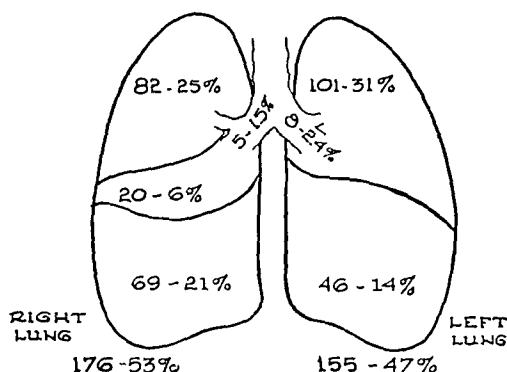


Fig. 4.—Anatomic location of lesion in 331 cases in which resection was done.

physician. Cough is without a doubt the commonest manifestation but is frequently disregarded because it has existed for some time and is thought to be due to irritation from cigarette smoking. Whereas it is true that cigarette smoking can produce a cough and expectora-

12. Graham, E. A.: Primary Cancer of the Lung with Special Consideration of Its Etiology, *Bull. New York Acad. Med.* 27: 261, 1951.

tion, any change in the cough should be considered of significance. Ninety per cent of our patients in whom resections were done had a cough, and in 55% it was the first symptom (Fig. 5). Not infrequently the earliest manifestation of a bronchogenic carcinoma is a respiratory tract infection. A lower respiratory tract infection which does not subside as it normally should suggests a possibility of bronchogenic carcinoma. In 55% of our

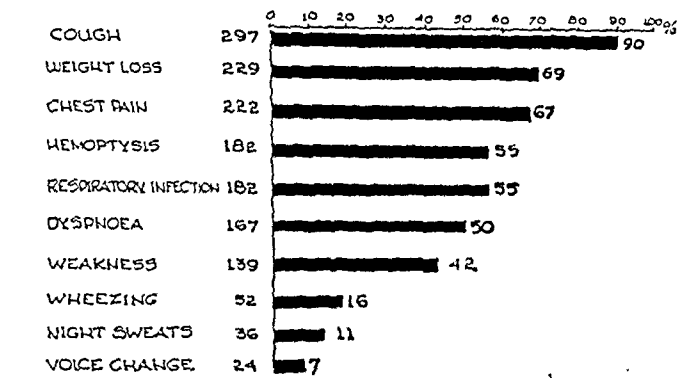


Fig. 5.—Symptoms on hospital admission in 331 patients in whom resection was done. Average duration was 12.3 months.

cases there was a history of a previous respiratory tract infection which was diagnosed either as influenza, viral pneumonia, or nonspecific pneumonitis, and it was the first manifestation in 22%. In each instance there were persistent symptoms after recovery from the acute infection. Hemoptysis is a manifestation which should never be disregarded, and although, when occurring in a man past 40, it does not necessarily mean bronchogenic carcinoma, it is a symptom which must be thoroughly investigated. It was present in 55% of our cases. Thoracic discomfort in a person who previously was well also demands investigation. Initially it is merely a consciousness of one's chest and not pain. The development of wheezing in a person, particularly in a man past 40, is suggestive of bronchogenic carcinoma because it means bronchial obstruction. An unexplained thoracic discomfort in any man past 40 must be thoroughly investigated to exclude bronchogenic carcinoma. Voice change which is the result of involvement of the recurrent laryngeal nerve fortunately occurs infrequently, because it represents extension beyond the lung. It was present, however, in 7% of our patients in whom resections were done. Whereas it has been believed by many to represent a contraindication to operation, we have not considered it as such. Although realizing that recurrent laryngeal paralysis means extension to the mediastinum and the recurrent nerve, it does not mean necessarily that resection cannot be done. Similarly, we do not believe that phrenic nerve paralysis should be considered a contraindication to exploration.

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The late manifestations of primary cancer of the bronchus are fever, pain, digestive disturbances, and emaciation and represent infection, breakdown of the tumor and extension to other structures. Therefore, they are of little significance as regards early diagnosis or effective treatment.

DIAGNOSIS

Because the symptoms of bronchogenic carcinoma occur so insidiously, it is hoped that an increasing use of routine chest x-rays every six months in men past 40, particularly in heavy smokers, will detect many cases of bronchogenic carcinoma before symptoms occur. Rigler¹³ states that peripheral lesions are invariably demonstrable roentgenographically before symptoms and signs are present. Scamman¹⁴ reports that in a total of 536,011 small chest x-rays, 43 cases (7.8 per 100,000) of bronchogenic carcinoma were detected. Overholt¹¹ in 14 chest lesions detected on mass chest surveys reported 35 cases of primary lung cancer. Boucot¹⁵ found in 156,920 persons surveyed 34 malignant lesions (1 per 5,000). She also found that in a survey of 40,660 apparently healthy workers in industry, 0.14% had primary lung neoplasm. Because of this, she advocates that "because of the prevalence of lung cancer among men over 45 years of age this particular group should be checked every six months whenever possible." Sillescu¹² found that lesions detected by x-ray must be considered as possible bronchogenic carcinoma, especially in men past 40. Effler, Blades, and Marks¹⁶ found that of 24 such lesions detected in military personnel 4 were malignant. O'Brien, Tuttle, and Ferkarey¹⁷ in 21 patients with solitary pulmonary shadows reported 8 (38%) with bronchogenic carcinoma. Husfeldt and Carlsen¹⁸ found four bronchogenic carcinomas among 33 cases of solitary pulmonary nodules. Sharp and Kinsella¹⁹ in a series of 96 cases isolated pulmonary nodules, of which 55 were histologically verified, found 11 bronchogenic cancer. Whereas it is possible for a symptomatic lesion to be situated that it would not be demonstrable on an x-ray

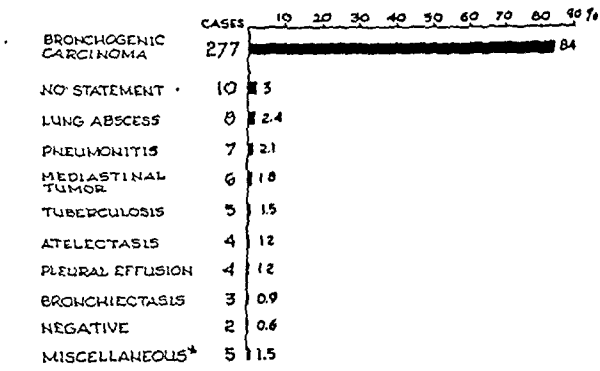


Fig. 6.—Roentgen diagnosis of 331 cases in which resection was done. * Indicates empyema, fibrosis, congenital cystic disease, lymphoblastoma and elevation of diaphragm.

of the chest, such is unusual. Because the resectability incidence is so high in asymptomatic lesions (100%, with 75% showing no lymphatic spread¹¹) and is so low in patients with symptoms (35% in our series, 70% which already had extension beyond the lung), it can be overemphasized that every pulmonary shadow must be viewed with suspicion and exploration insisted upon much more frequently than previously.

In patients with symptoms the diagnosis of bronchogenic carcinoma is usually not difficult if one only thinks of its possible existence. One of the most valuable diagnostic methods is roentgenography, not only because of the ease with which it can be performed, but also because it gives a high percentage of abnormal findings (Fig. 6). Roentgenography will demonstrate a shadow produced by the tumor resulting from infiltration

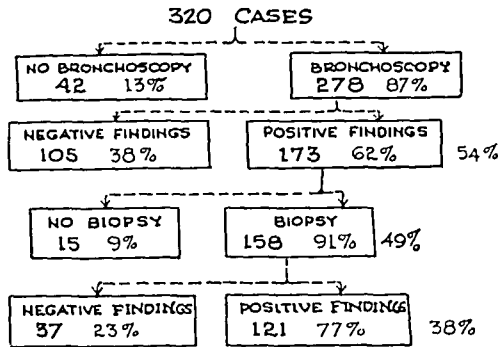


Fig. 7.—Results of bronchoscopic examinations in 320 cases in which resection was done.

of the pulmonary parenchyma or by atelectasis. The latter occurs whenever a bronchus is completely occluded by the tumor; air cannot pass beyond the site of the obstruction, and air from the alveoli distal to the tumor is absorbed. In this instance the shadow produced is much greater than would be produced by the tumor. It must be remembered, therefore, that all patients with massive shadows do not necessarily have extensive lesions. An even earlier roentgenographic manifestation is obstructive emphysema, which occurs as a result of an incompletely obstructing tumor of the bronchus. Because the bronchi are expansile and change their size during inspiration and expiration, a tumor which completely occludes the bronchus during expiration, at which time the bronchus is contracted, incompletely occludes the bronchus during inspiration, thus permitting the entrance of air into the bronchus and lung distal to the tumor but not permitting the exit of air during expiration. In this way an overdistention of the lung distal to the tumor occurs. In the present series of cases in which resection was done, a bronchogenic carcinoma was suspected roentgenologically in 84%, demonstrating the high incidence of correct diagnoses by this method. In those lesions located in the upper lobe bronchi, bronchography may be of value in demonstrating a bronchial obstruction which is suggestive of a bronchogenic neoplasm.

Early in our experience with bronchogenic carcinoma, bronchoscopy was thought to be the most valuable method of diagnosis, but it is now generally accepted that although bronchoscopy should be done in all instances, the percentage of carcinoma diagnoses made by this procedure is relatively small because most bronchogenic cancers are either in the periphery or in the upper lobe bronchi. Bronchoscopy should be done in every instance, however, not only because a biopsy study can be made of the lesions which are visible, but also because considerable information can be obtained by inspection of the trachea, carina, and the main stem bronchi, which may

be of value in determining operability. However, in the present series, a diagnosis of carcinoma was made bronchoscopically in only 38% of the cases (Fig. 7).

A relatively newer method, cytological examination of sputum or bronchial secretions, has become a most valuable diagnostic procedure and should be employed in all suspected cases. In 112 cases of proved primary cancer of the lung in our series, cytological examination indicated cancer in 76 (68%). There was only one false indication. This is, however, a difficult diagnostic procedure. It requires the services of a very good pathologist, one trained in cytological diagnosis and also willing to spend many hours looking for malignant cells.

TREATMENT

The treatment of bronchogenic carcinoma is pneumonectomy with complete en bloc removal of all the mediastinal nodes. Although Churchill and Sweet²⁰ have recently emphasized the desirability of lobectomy, we are convinced that lobectomy is not the method of choice in the treatment of bronchogenic carcinoma and should be used only when a pneumonectomy is contraindicated. All patients with bronchogenic carcinoma should be carefully studied preoperatively to determine their pulmonary function, in order to evaluate their ability to withstand the removal of an entire lung. Unless pulmonary studies suggest that a pneumonectomy will not be tolerated, lobectomy should not be done. Only by pneumonectomy and en bloc removal of all the mediastinal nodes can a high incidence of cure be obtained, and it is just as essential to remove the mediastinal nodes in bronchogenic carcinoma as it is to remove regional lymph nodes in carcinomas elsewhere.

Unfortunately, largely due to the fact that the medical profession still considers bronchogenic carcinoma an infrequent lesion and does not consider it as a possibility in a man past 40 in whom a relatively insignificant and mild thoracic discomfort has developed, the diagnosis is frequently delayed. In fact, in our series, there was an average delay of 12.3 months from the onset. Less than 10% had symptoms of two months or less, and only 0.9% were asymptomatic. Probably because of this, 385

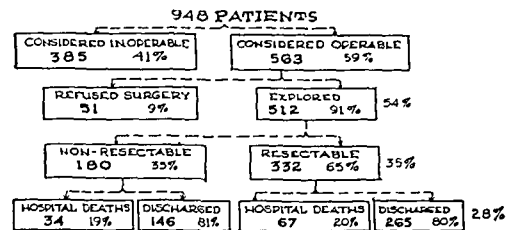


Fig. 8.—Results in the management of 948 patients with bronchogenic carcinoma.

(41%) of the 948 patients were obviously inoperable when first seen (Fig. 8). Five hundred sixty-three were considered operable, of which 51 (9%) refused surgery and 512 (91%) were explored (54% of the entire group seen). Of the 512 explored, resection could not be done in 180 (35%) because of extensive involvement of the

20. Churchill, E. D.; Sweet, R. H.; Soutter, L., and Scannell, J. G.: Surgical Management of Carcinoma of the Lung; a Study of the Cases Treated at the Massachusetts General Hospital from 1930 to 1950, *J. Thoracic Surg.* 20: 349, 1950.

heart or large vessels. Of this group 34 (19%) died in the hospital, the high mortality rate being due to associated disease and not to the exploration. Of the 332 patients in whom resection was done (65% of those explored and 35% of the entire group), 67 died in the hospital (20%) and 265 were discharged from the hospital (28% of the entire group).

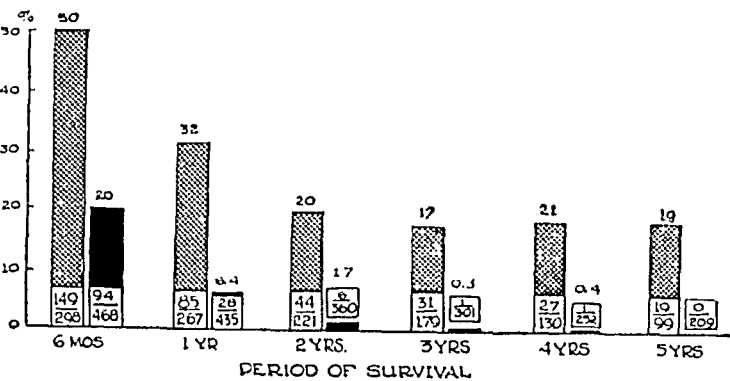


Fig. 9.—Comparison of survival rates in patients in whom resection was done and in patients in whom it was not done. Hatched bar indicates patients in whom resection was done and black bar, patients in whom it was not done. Figure in top half of white bar indicates number of patients alive; figure in bottom half, total number of patients.

It is interesting to compare the incidence of exploration and resectability in the private and Charity Hospital series. In 46% of the cases of the entire group, no operation was deemed advisable; exploration was done in 54% and resection in 35%. These same percentages in the private group were 34, 66, and 43%, respectively; while in the Charity Hospital series, they were 63, 37, and 23%, respectively. It is evident that the Charity Hospital patients are more likely to neglect themselves and are less likely to consult a physician, even though facilities are available to them at no cost. There has been a slight increase in the incidence of resectability throughout the years from 1935 to 1951, but this has been principally in the Charity Hospital series. Whereas resection was possible in only 8% of the patients at Charity Hospital in the period 1935 to 1941, resection was done in 33% from 1949 to 1951. These respective percentages in the private series are 42% and 49%.

Although 332 resections were done, unfortunately in most cases the lesion was extensive and had already in-

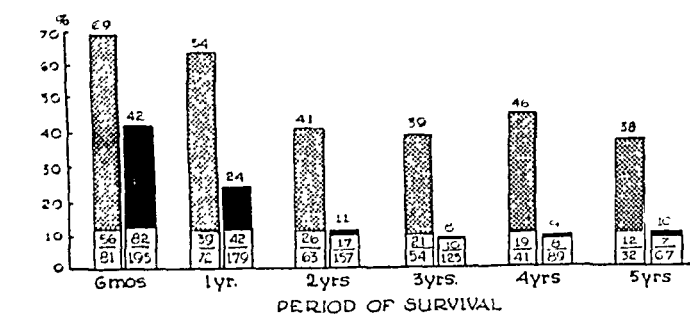


Fig. 10.—Comparison of survival rates after resection according to extension and localization of the lesion. Hatched bar indicates cases of localized disease and black bar, cases of extensive disease. Figure in top half of white bar indicates number of patients alive; figure in bottom half, number of patients in whom resection was done.

involved some other structure. In 232 the resection was termed a palliative resection, which means that the tumor had already extended beyond the lung, either to involve the mediastinal nodes or the mediastinal pleura, pericardium, heart, chest wall, or diaphragm. In only 90 cases was the lesion apparently limited to the lung. Ex-

tensive involvement necessitated extensive resection, as illustrated by the fact that 33 of the patients required intrapericardial ligation of the major vessels, 13 had suture of an auricle, 13 resection of a major portion of the chest wall, and 11 resection of a major portion of the diaphragm.

Although there was an over-all mortality rate of 20%, the mortality rate has decreased in more recent years. Whereas in the period 1935 to 1941 the mortality rate was 48%, from 1942 to 1946 it was 20%, and from 1947 to 1951 it was 17%. The decrease in mortality rate has been noticed particularly in the more advanced cases, in which there is extension of the carcinoma beyond the lung. The mortality rate in the cases in which the lesion was limited to the lung was 14% and in the cases in which it had extended beyond the lung, 22%. The mortality rate in the latter group in the period 1935 to 1941 was 63%; whereas in the period 1947 to 1951 it was 18%.

Of the 67 hospital deaths, 45% (30 cases) were due to cardiovascular disorders, of which most were cardiac disorders (25 cases). Thirty per cent (18 cases) were due to respiratory disorders, eighteen per cent (12 cases) to hemorrhage, and seven per cent to miscellaneous causes. The fact that the greatest number of patients were in the sixth decade of life, in which cardiovascular

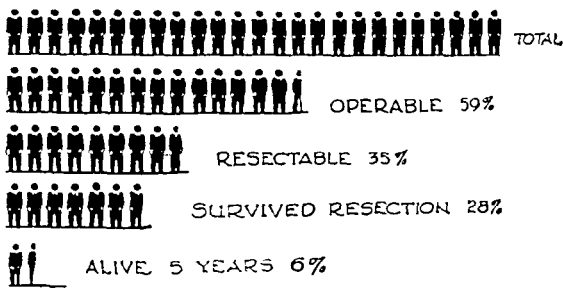


Fig. 11.—Management and results in 948 patients with bronchogenic carcinoma.

disease is prevalent, undoubtedly accounts for the high incidence of cardiovascular deaths, and there will always be an irreducible minimum of deaths from this cause. Because of this, it is imperative that careful cardiovascular surveys of all patients with bronchogenic carcinoma should be made before operation in order to reestablish good vascular function.

The period of survival of patients subjected to resection can be seen in figure 9. These figures are significant because they do not take into consideration deaths from other causes, and since most of these patients were of advanced ages, deaths from other causes are likely. It is our belief, however, that only by considering the survivals after a period of time can one evaluate the results obtained. It is of interest that whereas there is a rapid decrease in the survival rate for two years following pulmonary resection, a plateau is reached after that period of time, and approximately the same percentage are alive at the end of five years as were alive at the end of two years. In other words, a patient who has survived for two years following a pneumonectomy for bronchogenic carcinoma has a good chance of being alive at the end of five years.

As might be imagined, there is a good deal of difference between the curative and palliative resections. Of

e patients in whom "palliative resection" was done, 19% were alive at the end of six months, as compared with 69% of those in whom curative resection was done (Fig. 10). At the end of a year these respective percentages were 24% and 54%. At the end of five years they were 10% and 38%. It is thus seen that even among the advanced patients who are treated by pneumonectomy, 1 out of 10 is alive at the end of five years; whereas among those patients in whom there is evidence of gross extension beyond the lung, approximately 4 out of 10 are alive at the end of five years.

The value of resection in bronchogenic carcinoma is illustrated when one compares the survival rates obtained in the group of patients submitted to resection with the survival rate of those patients in whom resection was not done. Obviously the latter group is composed of much more advanced patients, generally because they were either inoperable when first seen or the lesion was not resectable when operated on. However, there were patients in whom the lesion appeared clinically resectable but who refused operation. All patients who were not subjected to resection were treated with other therapeutic palliative procedures, such as x-ray, nitrogen mustard, other chemotherapeutic agents, or a combination of all. Whereas at the end of six months 50% of the group in which resection was done were alive, only 20% of the group in which resection was not done were alive (Fig. 9). At the end of a year these respective percentages were 32% and 6.4%; at two years, 20% and 1.7%; three years, 17% and 0.3%. One patient out of 252 whom resection was not done survived four years, but died shortly thereafter. No patient survived five years;

whereas 19% of the patients subjected to resection were alive at the end of five years.

The results from treatment of bronchogenic carcinoma are not as satisfactory as they should be because of our 948 patients only 59% were operable, 35% were resectable, 28% survived resection, and only 6% were alive at the end of five years (Fig. 11). This is, indeed, a low salvage rate, but is undoubtedly due to the fact that there was considerable delay in the establishment of diagnosis and the institution of radical therapy. The fact that an average of over a year elapsed from the onset of the first symptoms until therapy was instituted accounts for the low incidence of resectability and the extremely low incidence of five-year salvage. It is our belief that as soon as the profession becomes cognizant of the frequency of bronchogenic carcinoma and considers the possibility of its existence in all men past 40 who have an unexplained thoracic discomfort earlier diagnoses will be made. It is also our hope that with an increasing interest in screening methods, such as mass chest roentgenography, many lesions will be detected before the patient has any clinical manifestations of the condition. As has been shown by Overholt and others,²¹ the incidence of resectability in this group can approach 100%. It is further hoped that physicians will urge all patients, especially men past 40 who smoke heavily, to have thoracic roentgenography done every 6 to 12 months and that whenever a shadow is detected prompt exploration should be done if bronchogenic carcinoma cannot be excluded within a short period of time.

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EFFECT OF CANCER ON LIVER ENZYMES

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There are two general approaches that the chemical analyst may employ in the study of malignant disease. The first of these is the direct chemical analysis of tumors, and comparison of such findings with those obtained in identical fashion on normal tissues and organs. The second approach is the chemical analysis of the tissues, circulating fluids, secretions, and excreta of cancerous patients, and comparison of such findings with those obtained on the same materials from normal persons. In the former case, it is expected that such information will yield a picture of the chemical processes inherent in the neoplastic transformation of tissues. In the latter case, it is expected that such information will give a description of the systemic effects induced by a tumor on the host that bears it, at a site or sites removed from the tumor, and in a state free of metastatic involvement. It is with this second of the chemical analytic approaches that this paper will deal.

Many striking and clear-cut phenomena have been noted in the study of the effects induced in the cancerous patient as a consequence of the presence of a tumor. The unhappily familiar cachexia of patients with advanced neoplastic disease is a clinical symptom of these effects,

sometimes exaggerated, sometimes partly masked, as a result of secondary causes, such as bacterial infection, generalized toxemia, malnutrition, and psychic depression, but nevertheless fundamentally due to systemic alterations produced by the tumor on the host. In view of the complexities involved in the study of such effects in the human patient, a great deal of the efforts in this area of cancer research has been conducted on experimental animals.

EXPERIMENTAL APPROACH

The experimental studies that my colleagues and I undertook several years ago were essentially naive and empirical.¹ We investigated a number of chemical and enzymatic systems under the same conditions in the tissues of normal and of cancerous experimental animals which were located at a distance from the tumor. Most of the tumors borne by these animals were of the trans-

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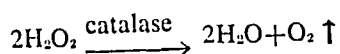
1. Greenstein, J. P.: *Biochemistry of Cancer*, New York, Academic Press, Inc., 1947.

planted variety, thus insuring their malignant character. None of the tissues studied had any metastatic involvement. The animals were in good nutritional status and were free of infection. Animals with tumors of all sizes and of different rates of growth were studied. As controls, normal and pregnant animals were employed, as well as animals bearing subcutaneous implants of rapidly growing embryonic minces. Thousands of animals were used in these studies.

Only those chemical systems were studied that were capable of being described in precise terms. Comparison in the level of these systems in the tissues of normal and of cancerous animals was placed on the following basis. The animals were decapitated and bled, and the tissues immediately excised and ground to a fine homogenate. The homogenate was taken up to a known volume either with distilled water or with buffered saline solution. An aliquot of the suspension was then mixed with the desired compound whose chemical transformation was to be studied, and the rate of this transformation followed by an appropriate experimental device. This rate is proportional to the amount of enzyme present in the tissue and presumably specific for the compound added.

It would be most desirable to make the comparison between such rates in two kinds of tissues on the basis of the rate per cell of each tissue. This is not readily feasible. Since it is presumed that all cells on the average, of a liver for example, yield the same amount of extractable nitrogen as all cells, on the average, of another liver of an animal of the same species, age, sex, and general physical condition, we have made the comparison between rates of comparable tissues on the basis of unit nitrogen. Obviously a normal liver and a cirrhotic, or fatty-degenerated, liver could not be compared on this basis. In our experimental animals, with or without tumors, the comparable tissues were microscopically indistinguishable. Our aim to observe how each cell, or unit volume, or unit mass, of a tissue responds to the presence of a distant tumor is only approximately served by the device of basing this change on a unit weight of nitrogen, and, although we are aware of this approximation, we cannot, despite all other bases proposed, think of a better device.

Early in this study we noted, with some surprise, that nearly all enzyme systems in all the tissues studied were at very nearly the same level in normal and in cancer-bearing animals. Only one system, and that in the liver, appeared to be markedly affected by the presence of a cancer elsewhere in the animal. This system was found to be catalase, a finding already anticipated by Brahn, who worked with human material and who reported his findings in 1916.² Catalase is a hematoporphyrin enzyme that acts on hydrogen peroxide to decompose it to water and molecular oxygen, thus:



The level of this enzyme in tissues was followed by mixing the homogenate with hydrogen peroxide and measuring the rate at which oxygen gas was evolved. When liver homogenates prepared under identical circumstances from normal animals and from cancer-bearing animals

were compared, the rate of evolution of oxygen gas from added peroxide was always less for the latter animals than for the former. The degree of difference between the livers from the two sources varied considerably with the experimental conditions (the concentration of peroxide, temperature) but in any event there invariably appeared to be more catalase activity per unit of nitrogen of tissue in the livers of normal animals than in the livers of those with such diverse tumors as lung carcinomas, breast carcinomas, fibrosarcomas, and bone tumors.

In the face of this invariable finding of a diminished catalase level in the livers of cancerous animals was the equally constant finding of normal levels of cytochrome oxidase, cytochrome C, peptidase, dehydropeptidase, amino acid oxidase, acid and alkaline phosphatase, ribonuclease, desoxyribonuclease, and xanthine dehydrogenase. These symptoms remain at a normal level in livers of cancerous animals which simultaneously reveal a marked diminution in the catalase level. Under conditions of severe starvation and of infection, the total liver proteins diminish and all of these symptoms are reduced in magnitude. Only in the cancerous animal is the catalase system affected.

Three tissues in the animal body have a notably high level of catalase activity. These are liver, kidney, and erythrocyte. Although in the cancer-bearing animal the liver catalase activity is markedly depressed, that of the kidney is little if at all affected, while the erythrocyte catalase is not affected at all.

EFFECT OF GROWTH RATE OF TUMOR

In general, the reduction of the liver catalase level is noted only in animals bearing rapidly growing tumors and is readily observable when the tumor weight is at least about 5% of the body weight of the animal. With slow-growing tumors, the liver catalase activity is apparently normal. It is possible to conceive of a competitive aspect involving the toxic effect of the presence of the tumor and the repair mechanism of the liver, whereby the former predominates in the case of rapidly growing tumors and the latter in the case of very slow-growing tumors.

REVERSIBLE EFFECT OF TUMOR

Rats when inoculated subcutaneously with a rapidly growing transplanted tumor demonstrate a proportionate decrease in their liver catalase level with growth of the tumor. When such animals are anesthetized and their tumors surgically removed, the liver catalase level is restored to normal levels within 48 hours. Reinoculation of the tumor produces another fall in the liver catalase level, followed by a second restoration when the tumor is excised.

Mice inoculated intracaudally with a rapidly growing tumor also show a proportionate decrease in liver catalase activity levels, which are restored to normal at caudectomy. Other strains of mice inoculated intraperitoneally with a tumor which grows rapidly for a while, and then spontaneously regresses, also show a diminution in liver catalase during the period of growth of the tumor, followed by a gradual restoration to the normal level during the period of tumor regression.

Thus, no matter at what site the transplanted malignant tumor is grown in the animal, the liver catalase

2. Brahn, B.: Further Researches on the Enzymes in the Liver of the Cancerous, *Sitzungsber. kgl. Preuss. Akad. Wissensch.* 20: 478-481, 1916.

activity will diminish if the tumor grows fast enough, and no matter how the tumor is removed, the liver catalase activity will come back to normal. The effect of the tumor on the liver is therefore reversible.

EFFECT OF GROWING EMBRYO

Embryonic minces when implanted subcutaneously in mice of the same strain will grow progressively and rapidly for several weeks and then spontaneously regress and disappear. Such mice during the period of rapid growth of such minces, or pregnant mice near term, all possess a normal liver catalase activity. The effect on the liver catalase activity is not due, therefore, to a growing tissue per se, but to a growing tissue which is a tumor.

IN VITRO STUDIES

Homogenates of normal liver and of tumors mixed together in a test tube have a catalase activity that is the sum of the catalase activities of both tissues. Neither has an effect on the other when mixed in a test tube. The effect noted is apparently only in the living animal.

EVIDENCE FROM OTHER INVESTIGATORS

Weil-Malherbe and Schade,³ with the tentative premise that the fall in liver catalase activity might be caused by the high protein requirements of a rapidly growing tumor, studied the progressive decrease of the activity in two series of cancer-bearing rats maintained on a high or low protein diet. Regardless of the nature of the diet, however, the liver catalase activity of the tumor-bearing animal was consistently lowered. Dounce and Shanewise⁴ have confirmed the finding of a lowered liver catalase activity in tumor-bearing rats, and in addition, have noted that the same effect occurs in rats infected with leprosy bacteria.

Von Euler and Heller⁵ made a study of the distribution of catalase activity in the cytoplasm and formed elements of the liver cells of normal and tumor-bearing rats, and noted that (a) catalase in normal animals is nearly equally divided between mitochondria and microsomes, and (b) with growth of the tumors, the loss in liver catalase at first occurs chiefly in elements other than the mitochondria, but in later stages of tumor growth the mitochondrial catalase also appreciably diminishes in activity. The presence of the tumor, however, did not apparently affect the amount of the formed elements of the liver cell, as measured by their total nitrogen content.

One of the most extensive recent studies in this field is that of Adams,⁶ who noted that, with the subcutaneous injection of a homogenized fibrosarcoma into two strains of mice, the liver catalase activity fell significantly at 24 and 48 hours, rose to normal by the fourth day, and diminished again markedly thereafter. Injection of normal tissues, including embryonic tissue, produced no effect on the liver.

Further studies of the toxic effect of growing tumors in the animal on its tissue catalase level were made by Appleman, Skavinski, and Stein,⁷ who noted the much greater decrease in the liver catalase level than in the kidney or erythrocyte level (which were practically normal). These authors also noted an enlargement of the liver in cancerous rats. Together with the observation of the decreased liver catalase level in cancerous animals, Begg⁸ noted an enlargement of the adrenal with loss of ascorbic acid and cholesterol.

The observation that, per unit weight of tissue or per unit weight of nitrogen, the catalase activity of the livers of tumor-bearing experimental animals is markedly and uniquely depressed below the normal has now been made in laboratories all over the world. The mechanism of this effect is still somewhat obscure. Conceivably, the effect might be due to some toxic material elaborated by the tumor, which by traveling through the circulation affects the synthesis or storage of catalase in the liver, or it might be due to some abstraction by the tumor of some material essential for such synthesis or storage. A very significant contribution to the solution of this problem was made recently in Japan.

ISOLATION OF "TOXOHORMONE" FROM TUMORS

In 1949, Nakahara and Fukuoka⁹ reported the isolation of a protease-like material from human cancers which, when injected intraperitoneally into mice, produced a marked diminution in their liver catalase. This material was water-soluble and alcohol-insoluble and had no effect in the test tube on homogenates of normal liver. Later studies showed that similar materials could be obtained from mouse tumors.¹⁰ Greenfield and Meister,¹¹ in an extensive fractionation study, showed that only catalase of several systems investigated was markedly lowered in the livers of mice given intraperitoneal injections and that two days after such injections the liver catalase activity was restored to normal. Most recently, Nakahara has reported that the effect of the injection of this tumor fraction, to which he has given the designation "toxohormone," can be neutralized by the injection of iron salts.¹² It would appear that this material might produce its effect on the lowering of liver catalase by combining with iron and, in some way, abstracting it from the circulation, thus limiting the synthesis of the iron-containing catalase molecules.¹³

CONCLUSION

A great deal of effort has been expended in many laboratories in the study of a single enzyme, catalase, in liver as affected by the presence of a tumor in a distant site. Its value at the moment is only theoretical. But it is one of the established phenomena of cancer. Its future practical significance on a clinical level must await further experimentation.

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DRUG PROPHYLAXIS OF AMEBIASIS

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Amebiasis is well recognized as a problem in institutional groups, and the occurrence of the infection in mental hospitals, particularly among highly disturbed patients, has been described repeatedly.¹ The problem of control presented by these situations is difficult. Clinical cases and high carrier rates usually persist even when the environment is assiduously sanitized to minimize the hazard of transmission through food, milk, water, or fomites, such as eating utensils, clothing, and bedding. The regulation of the personal hygiene of patients, which is frequently complicated by fecal incontinence and coprophagy, is fraught with obvious inherent difficulties. Under such circumstances the attainment of even partial control of transmission of amebiasis is contingent on minimizing both the excretion of cysts of *Endamoeba histolytica* and the environmental fecal contamination.

The situation in which the present studies were conducted is illustrative of the magnitude of the epidemiological problem of amebiasis inherent in a particular category of institutionalized subjects. An opportunity for examination of the possible usefulness of mass chemotherapy and chemoprophylaxis in the control of amebic infestation of such a population was given.

Of the antiamebic drugs currently available, those which are most effective in clearing *E. histolytica* from the intestine are ineffective against extraintestinal foci, and those which are effective in the treatment of hepatic amebiasis are unreliable agents against intestinal amebiasis.

Because intestinal amebiasis may be cured without affecting incipient hepatic infection, optimum control would require a therapeutic regimen directed against both intestinal and extraintestinal amebiasis.² For the purposes of this study, bismuth glycolylarsanilate (milibis³), an effective intestinal amebicide,³ and chloroquine phosphate (aralen⁴ diphosphate), a highly effective drug for the treatment of hepatic amebiasis⁴ as well as malaria,⁵ were combined in a tablet comprised of 250 mg. of bismuth glycolylarsanilate and 75 mg. of chloroquine phosphate.⁶

From the Sterling-Winthrop Research Institute, Rensselaer, N. Y. (Drs. Berberian and Dennis); the Bureau of Epidemiology and Communicable Disease Control, Division of Medical Services, New York State Department of Health (Dr. Korn); and the Wassaic State School, Wassaic, N. Y. (Dr. Angelo).

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6. The bismuth glycolylarsanilate and chloroquine phosphate were provided by Winthrop-Stearns, Inc. and the tablets were prepared by the Sterling-Winthrop Research Institute.

7. These surveys were made in connection with other studies by a team of investigators from the National Institutes of Health, Bethesda, Md. Reports are on file in the New York State Health Department.

MATERIALS AND METHODS

Study Population.—During the investigation of clinical amebic dysentery in one building at the Wassaic State School, Wassaic, N. Y., it became apparent that, although clinically recognizable illness due to *E. histolytica* was not occurring in other buildings, infection with this parasite was widely spread throughout the institution, which houses some 5,000 mentally deficient patients. Stool surveys carried out in 10 representative buildings⁷ showed that the carrier rates were high and were more or less parallel to the degree of mental deficiency and the related quality of personal hygiene of the patients. Among patients of low grade mentality the observed prevalence of carriers was 55%, compared with 17% among patients with high grade mentality; whereas the carrier rate among employees scattered throughout the institution was only 4%.

Two infirmary buildings, "O" and "P," presented a situation which appeared appropriate for mass chemoprophylactic studies. Building "O" housed 229 male inmates having a median age of 15 years. Building "P" housed 207 male inmates, whose median age was 25 years. The mental caliber of the inmates of both buildings was extremely low; about 10% were bedridden. In each building the ambulant patients intermingled in a single large room during the day and were housed in four separate wards at night. The records indicated that some 80% of the subjects exhibited fecal and urinary incontinence from time to time. Obviously, despite rigorous housekeeping measures to keep the environment clean, it was impossible to prevent completely the transfer of the more hardy fecal borne infections. In neither of these buildings had clinical amebiasis been recognized during the past decade, and bacillar dysentery apparently had been absent for at least four years. The two buildings were served by the same central kitchen supplying the rest of the institution for the main meal of the day, but breakfast and supper were furnished from a separate kitchen in each of the two buildings. Careful sanitary survey of the premises satisfactorily excluded the likelihood that amebiasis was being spread through water, milk, or food. On the other hand, the strong fecal odor in the buildings was almost sufficient to prove, in a crude way, the more probable routes of transmission. Frequent baths, accompanied by changes of clothing and linen, and daily scrubbing of floors and walls failed to eliminate fecal contamination and odor. It was in this milieu that the study described below was carried out.

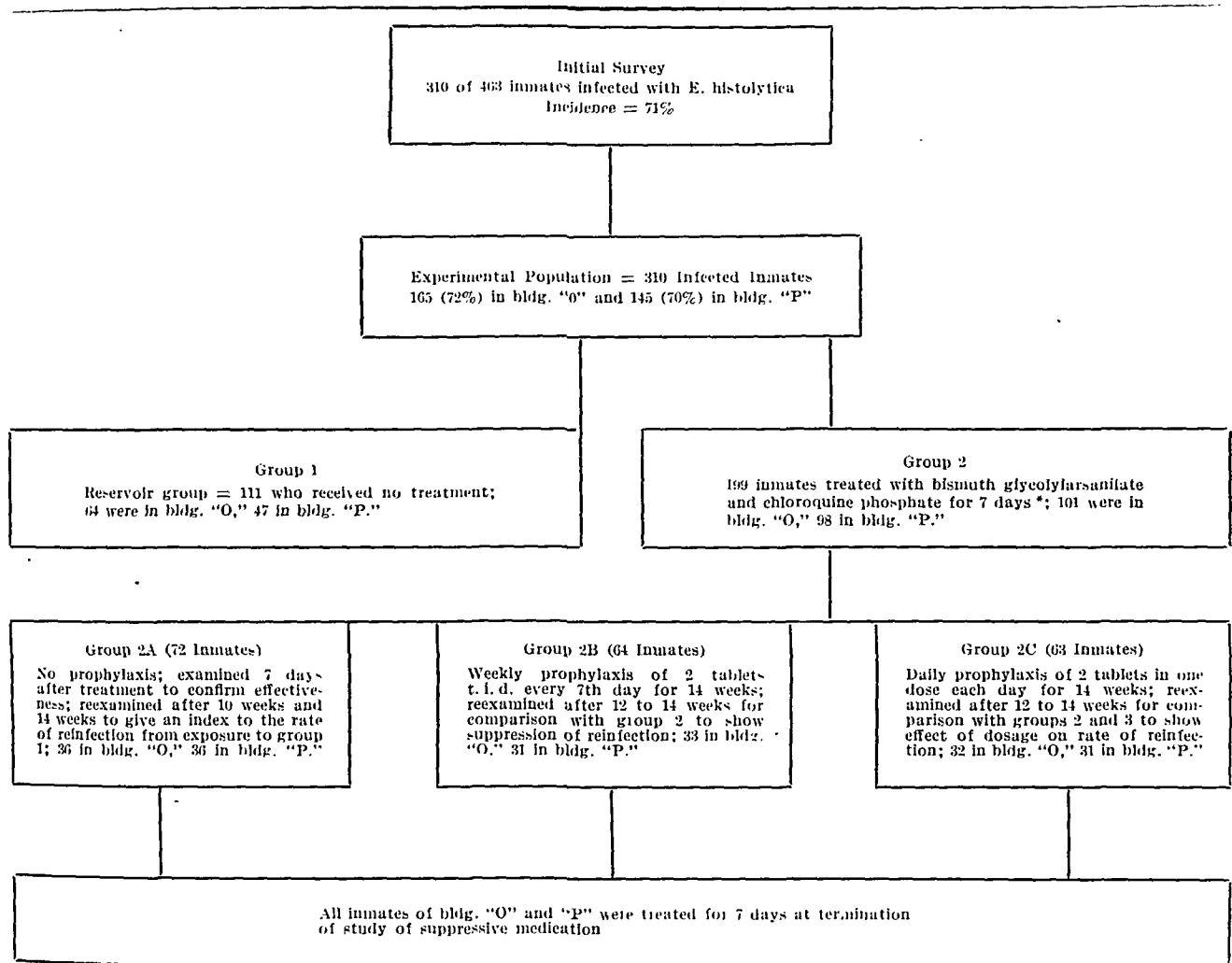
Laboratory Procedures.—The diagnosis of infection with *E. histolytica* was based on examination of samples of casual stool specimens. The specimens were sealed in waxed cups with fitted covers, labeled with an identifying code, and transported to the laboratory at the Sterling-Winthrop Research Institute at Rensselaer. The stool specimen was approximately 24 hours old at the

time of examination; hence diagnosis was based on demonstration of characteristic cysts. The zinc sulfate flotation procedure for concentration of cysts was used for all samples, and D'Antoni's iodine stain was used to facilitate microscopic examination. In some instances slides of fecal smears were fixed in Schaudinn's solution and stained with Heidenhain's iron hematoxylin. Also, the examination of some specimens was extended by culturing in Boeck and Drbohlav's medium.

On the first round of examinations, when hematoxylin-stained slides and culture were used as well as zinc

Design of Study.—The design of the study is shown diagrammatically in table 1. An initial survey was carried out in April, 1950. Because not more than three stools per patient were examined, it was recognized that all cases of infection would not be demonstrated, but the findings were adequate for the purposes of the study planned. A total of 436 persons were examined, of whom 310 (71%) yielded stools that were positive for cysts of *E. histolytica*. In building "O" the infection rate was 72%, and in building "P" it was 70%. Seventy per cent of the total number of infected subjects were detected on

TABLE 1.—Plan of Experiment



* All subjects weighing less than 80 lb received half doses. Juveniles were distributed proportionately in the experimental groups.

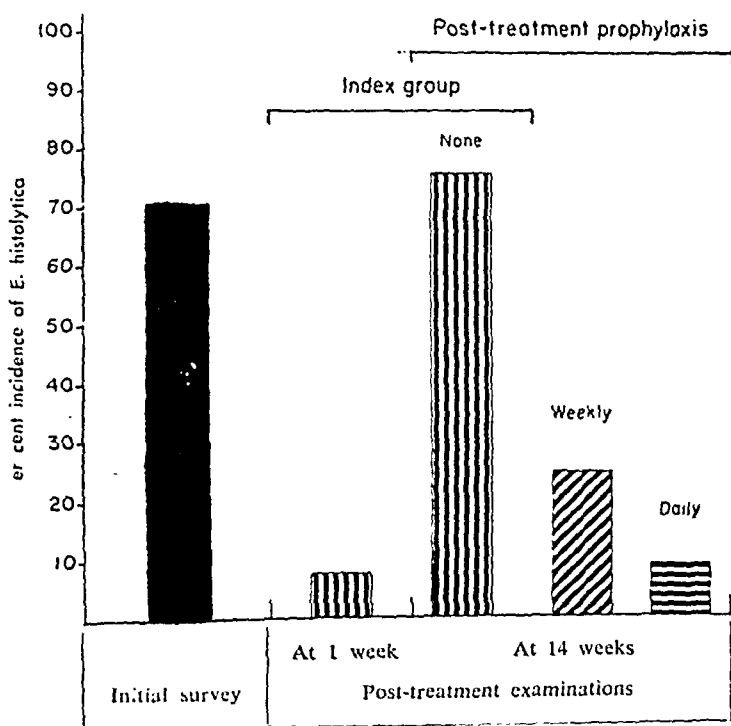
sulfate concentration the number of cases detected was not appreciably greater than when the concentration method was used alone. Hence, to conserve time, the concentration procedure was relied on for all subsequent examinations. For any given round of examinations (plan of experiment in table 1), samples of at least three stool specimens were thoroughly examined before a subject was diagnosed as not infected; if the first or second specimen was clearly positive, examination was discontinued; if the diagnosis was in doubt because of only rare atypical cysts, additional stools were examined. The same procedure was used for all follow-up examinations.

the first stool examination, an additional 13.4% were detected on the second stool examination, and 16.6% were detected on the third examination. Study of the carrier prevalence in each 5 year age group and according to the length of residence in the institution failed to show any significant variation; apparently the exposure to infection was so heavy that the effect of such factors was totally obscured.

The population of 310 inmates whose stools were positive for *E. histolytica* was divided into four groups by alternate selection from an alphabetical list of the patients, with care being taken to provide proportional dis-

tribution of those who were first reported infected on the first, second, or third stool specimen. As shown in table 1, group 1 was arbitrarily made slightly larger than the other groups and consisted of 111 inmates who were left without any form of antiamebic medication in order to provide a known source of exposure to reinfection. None of this group showed symptoms of amebiasis; hence the temporary withholding of medication was justifiable. Groups 2A, B, and C were comprised of 72, 64, and 63 persons, respectively.

In order to estimate the prophylactic effect of the proposed medication regimens, it was first necessary to reduce the incidence of infection in the experimental groups to a minimum. For this reason the 199 persons in groups 2A, B, and C were given a therapeutic course of bismuth glycolylarsanilate and chloroquine phosphate in combination tablets for seven consecutive days; the daily dosage was 2 tablets three times daily (after meals) for persons weighing 80 lb. (36.3 kg.) or more and half of this dosage for those weighing less than 80 lb.



Effect of medication with bismuth glycolylarsanilate and chloroquine phosphate on the incidence of *E. histolytica* in the presence of known sources of reinfection.

The members of the three groups given treatment were distributed proportionally throughout all wards of both buildings, so that subsequent exposure to infection by association with group 1 was reasonably uniform.

After the seven day course of therapy all persons comprising group 2A were reexamined to establish the therapeutic effect and to provide a reference point for demonstrating the frequency of reinfection during subsequent months. Group 2A served as the index of the rate of reinfection and/or relapse. On completion of the therapeutic course, the members of groups 2B and C were shifted to dosage regimens designed to demonstrate possible prophylactic or suppressive action of the medication. The 64 persons in group 2B were treated every seventh day with the equivalent of one daily dose of the initial therapeutic schedule, i. e., 2 tablets three times a day. The 63 persons in group 2C continued to receive the medicament daily, the dosage being 2 tablets at once

for those weighing 80 lb. or more and 1 tablet for those under that weight. Prophylactic medication was maintained for 14 weeks.

Eight weeks after completion of the therapeutic course, examination of a series of three stool specimens from each person in group 2A showed that 75% of this group again had stools positive for *E. histolytica*. It was decided, therefore, to study again all persons in groups 2A, B, and C to determine the effectiveness of the prophylactic medication in the presence of the known infected subjects of group 1. During the period from the 10th to 14th week of prophylaxis, a series of three stool specimens was submitted from each person in the three groups. All specimens were labeled by code number only, so that the persons concerned with examining the stools had no knowledge whatever as to which group was represented.

RESULTS

In addition to the post-therapeutic check-up on group 2, steps were taken to evaluate crudely the rapidity with which therapy took effect. For this purpose single stool specimens were collected from 36 persons on both the first and second day of treatment. Twenty-five, or 69%, of the specimens collected on the first day of treatment were negative for *E. histolytica* cysts. Stool specimens from the same 36 persons were collected on the second day of treatment, of which 32 (89%) were negative. Three of the four persons with positive stools on the second day had had negative ones on the first day. With minor variations, the effect of the medicament was quickly apparent.

Results of the prophylactic experiment are summarized in table 2 and the chart. As noted above, after completion of the seven day therapeutic course, stool specimens were obtained from 71 of the 72 patients in group 2A on the first, second, and sixth post-treatment day. Only 1 of the 71 first post-treatment day specimens was positive, 2 more were positive on the second post-treatment day, and an additional 2 were positive on the sixth post-treatment day. Thus, using three stool examinations as an index, only 5 of the 71 patients (7%) persisted in remaining infected, and these represent therapeutic failures. However, since four of these subjects had positive stools on only one of the three examinations, additional stools were obtained from these same subjects on the eighth and ninth post-treatment day; in only one patient (1.4%) was the stool persistently positive. It is apparent that within the limitations of the type of measurement used, the therapy was very effective (93 to 98.6% freed of infection).

When group 2A was reexamined after 10 to 14 weeks of exposure to the known infected persons of group 1, cysts of *E. histolytica* were demonstrated in 55 of the 72 subjects examined. The infection rate had increased from 7% or less to 76%. As shown in table 2, only 16 of the 64 subjects who had been receiving one-seventh of a therapeutic course of bismuth glycolylarsanilate and chloroquine phosphate at weekly intervals were infected, and only 6 of the 63 subjects who had been receiving medicament daily had cysts of *E. histolytica*. It is apparent that daily medication with a combination of 0.5 gm. of bismuth glycolylarsanilate and 0.15 gm. of chloroquine phosphate (adult dose) essentially resulted in

complete suppression of reinfection, since the observed infection rate of 10% was not significantly greater than the post-treatment residual rate observed in the index group. The weekly administration of a full daily dose (1.5 gm. of bismuth glycolylarsanilate and 0.45 gm. of chloroquine phosphate) was somewhat less effective in preventing reinfection with *E. histolytica*, but the infection rate was only one-third of that observed in the index group. In view of the heaviness of the exposure to a large reservoir of carriers, it is probable that the weekly medication regimen would offer a relatively high degree of protection against amebiasis under more casual conditions of exposure.

It should also be noted that during the course of the final survey three stools were examined from each of 74 patients selected at random from the 126 whose stools were originally negative for *E. histolytica*; in 36 (50%) the stools had become positive during the three month interim period.

Clinical Observations.—The inmates of the two experimental buildings were watched carefully during the period of medication with bismuth glycolylarsanilate and

COMMENT

The data presented above show that the combination of bismuth glycolylarsanilate and chloroquine phosphate was tolerated in therapeutic doses that produced stools that were negative for *E. histolytica* cysts in at least 93% of a group of patients after one week of medication. These results are comparable to data previously reported for the therapeutic efficacy of bismuth glycolylarsanilate alone.³ The amount of chloroquine phosphate administered would presumably eliminate any incipient extra-intestinal amebic lesions that would not be affected by bismuth glycolylarsanilate.⁶ It has also been shown that in the presence of heavy exposure to reinfection with *E. histolytica*, the weekly administration of one-seventh of a therapeutic course of the bismuth glycolylarsanilate and chloroquine phosphate combination reduced the reinfection rate by approximately two-thirds. The daily administration of one-third of that dose reduced the reinfection rate to a negligible level. Thus the chemoprophylaxis of amebiasis by means of bismuth glycolylarsanilate and chloroquine phosphate has been demonstrated to be a feasible procedure. It also should

TABLE 2.—*Suppressive Effect of Weekly or Daily Prophylactic Medication with Bismuth Glycolylarsanilate and Chloroquine Phosphate on the Incidence of E. Histolytica in 127 Subjects Constantly Exposed to 111 Known Carriers for Ten to Fourteen Weeks*

Experimental Group		Medication Regimen		Distribution by Dosage								
				Adults			Juveniles *			Total		
				No.	No. Infected	% Infected	No.	No. Infected	% Infected	No.	No. Infected	% Infected
2A	Index group,§ 1st week post-treatment	Infected	Not infected	54	4	7.4	17	0	0	71	4	7.0
2A	Index group, 10 weeks post-treatment	Infected	Not infected	55	42	76.0	17	13	76.0	72	55	76.0
2B	Prophylaxis, weekly for 14 weeks.....	Infected	Infected	49	12	24.0	15	4	27.0	64	16	25.0
2C	Prophylaxis, daily for 14 weeks.....	Infected	Infected	51	4	8.0	12	2	17.0	63	6	9.5

* Half dose administered to all subjects weighing less than 80 lb.
† Th. = therapeutic course, dose three times daily for 7 days.
‡ Pr. = prophylactic course following therapeutic course.
§ Treated to clear the stools of *E. histolytica* but not given prophylactic medication (to provide an index of the efficiency of treatment as well as the rate of reinfection for comparison with groups 3 and 4).

chloroquine phosphate in combination tablets. No clinical evidence of amebiasis was observed in the population. The persons receiving the medicament, both therapeutically and prophylactically, were checked continually for signs of untoward reaction, but none was observed other than the vomiting of the medicament by six patients during the initial one week therapeutic course. To those administering the drugs, it seemed likely that this vomiting was a response to the necessity for swallowing several tablets, rather than a specific toxic effect of the drugs. Medication was not discontinued in any of these patients, and no further difficulties were observed.

Because of the presence in these buildings of many patients who had epileptic seizures from time to time, detailed observations were made as to the extent to which seizures occurred in those receiving treatment. During the two week period following initiation of the therapeutic course, the median number of seizures in a group of 25 epileptics was only one, compared with a median of 23 seizures for these same persons during the previous 12 months. It therefore seemed unlikely that the treatment tended to accentuate the epileptic seizures. During the ensuing months no untoward reactions were observed among patients in the groups receiving daily or weekly prophylactic medication.

be noted that chloroquine phosphate, in either the weekly or daily prophylactic regimen used, is adequate for the suppression of malaria.⁶ It is apparent, therefore, that either of the regimens used in the current study would be expected to provide a high degree of simultaneous prophylaxis or suppression against both amebiasis and malaria under conditions in which both diseases are sufficiently common to represent a significant risk.

Obviously the environment and population studied are not comparable to the general population in this country, but heavy exposure to amebiasis is not uncommon in institutionalized groups or in some tropical and Asiatic communities. The evaluation of this disease control procedure was therefore made rigorous. These studies are being continued in a manner designed to determine the efficacy of chemoprophylaxis in populations that are exposed less often or less intensively to the infecting bacilli.

One wonders why clinically recognizable illness, particularly dysentery, was not observed in this highly infected population, but no adequate explanation can be offered. In an adjacent infirmary building, housing patients of the same age, mental status, and level of per-

8. Dennis,³ Conan.⁴

sonal hygiene, who were receiving exactly the same diet, a series of 11 typical cases of amebic dysentery occurred during a two month period just prior to institution of these studies. Two of the persons suffering from amebic dysentery died, one with liver abscess. The carrier prevalence of *E. histolytica* in that particular building was reported to be slightly lower than in buildings "O" and "P."

It has been pointed out that the amebicidal efficacy of poorly soluble bismuth glycolylarsanilate is reduced by diarrhea³; hence this drug, alone or in combination with chloroquine, should be used only after acute dysentery has been controlled; a single dose of emetine is usually sufficient to reduce peristalsis, although unreliable as an amebicide.

The factors responsible for the appearance of amebic dysentery in one group, while another infected group remained asymptomatic under seemingly identical circumstances, are so obscure as to merit special intensive study. Conclusive evidence is lacking that some strains or races of *E. histolytica* are inherently more invasive than others.

SUMMARY

The administration of 6 bismuth glycolylarsanilate (milibis®) and chloroquine phosphate (aralen®) combination tablets (0.25 gm. of bismuth glycolylarsanilate and 0.075 gm. of chloroquine phosphate) a day for seven days as a therapeutic course was rapidly effective in producing stools which were negative for cysts of *E. histolytica* in at least 93% of the subjects examined. In the presence of intense exposure to a known reservoir of infection of three months, post-treatment prophylactic administration at weekly intervals of 6 tablets (adult dose) reduced the infection rate to 25%, and daily administration of 2 tablets reduced the infection rate to 10%, compared with a reinfection rate of 76% in the control group. Untoward toxic manifestations from the medicament were not observed. The chemoprophylaxis of amebiasis by administration of bismuth glycolylarsanilate and chloroquine phosphate in combination was demonstrated to be a feasible procedure. Simultaneous chemoprophylaxis of amebiasis and malaria is suggested as an attainable objective, with either of the medication regimens studied.

CLINICAL MANAGEMENT OF "FUNCTIONAL" DISORDERS

THE DIAGNOSTIC INTERVIEW

Malcolm S. M. Watts, M.D.

and

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The understanding and sympathetic physician realizes at almost every patient who consults him is worried and anxious. Sometimes the cause of the patient's anxiety is obvious; often it is not. A patient with a fracture or one who has noticed gross blood in the stool is understandably disturbed. His anxiety often results in symptoms which are in addition to those of the underlying pathological process. Such anxieties, however, present little difficulty to the clinician. The symptoms are recognized for what they are and respond rapidly to reassurance, mild sedation, and effective treatment of the obvious disease or injury.

On the other hand, many patients come with anxiety of more obscure cause. It may manifest itself as fatigue, nervousness, tenseness, headache, insomnia, indigestion, or a host of other symptoms. It is with this group that this paper is particularly concerned. Such patients are frequently seen by physicians engaged in the practice of medicine, surgery, or other clinical specialties. Often a thorough diagnostic study is carried out, and if no "cause" is found for the patient's symptoms, both the physician and patient become discouraged or disgusted.

There is reason, however, to adopt a more optimistic attitude toward many of these patients. Actually, there are more hopeful avenues of approach to the management of "functional" disorders than is the case with most

"organic" diseases. Psychologically, if the underlying emotional difficulty is recognized, the patient may make a better adjustment, with subsequent improvement in his symptoms. Somatically, there is a large armamentarium of drugs and other treatment which may be used to diminish symptoms. Socially, the physician is often able to modify the patient's environmental situation in such a way as to reduce anxiety and tension.

The task of the busy physician who treats patients who have functional symptoms is to reach the root of the difficulty and to work out an effective plan of treatment in the time he can afford to devote to a single patient. Sometimes this is easy. A woman plagued by fear that she has cancer may be completely relieved by simple assurance after careful palpation of the breasts or examination of the cervix uteri. More often the problem is not so simple, and at times it may be difficult indeed.

THE WORD "FUNCTIONAL"

Unfortunately no single word or term has been generally accepted to designate the kind of disorder under discussion. The symptoms have been described many times. Anxiety, irritability, inability to relax, morning fatigue, mental conflicts, difficulty in making decisions, and symptoms specifically related to dysfunction of various organ systems, particularly the gastrointestinal or cardiovascular systems, are common. Patients with these complaints have been classified as being either in a state of tension or in a state of fatigue. Other authors have

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used the terms benign nervousness, anxiety state, chronic nervous exhaustion, psychoneurosis, tension state, and “relatives of the insane.” None of these terms seems entirely satisfactory.

It has been pointed out that all patients who have symptoms of “nervousness” may exhibit concomitant physiological dysfunction of many organ systems, including the cardiovascular, gastrointestinal, respiratory, genitourinary, and endocrine. Inasmuch as these are all related to a disturbance in the function of the patient as a whole, the term “functional” may be used to describe these disorders. It is in this sense that we use the word.

CAUSE OF FUNCTIONAL DISORDERS

It may be stated simply that in a person who does not make a healthy adjustment to psychological conflict symptoms of functional disorders eventually develop. Conversely, a patient with a functional disorder always has a psychological conflict at the root of his troubles. In simple terms, a psychological conflict may be said to exist whenever a situation is different from that which the patient would like. Conflicts may be on a conscious level, within the awareness of the patient, or they may be totally unconscious and not recognized by the patient’s conscious mind. In either case the patient may not be aware of any connection between the psychological conflicts and the symptoms of which he complains.

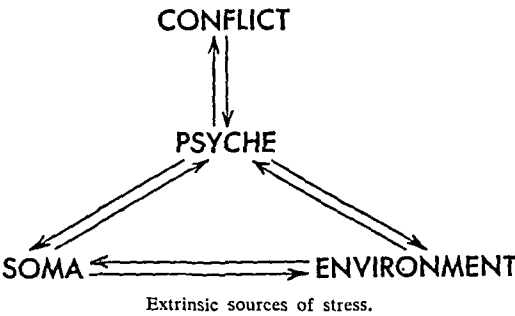
Physical symptoms associated with these psychological or emotional disturbances are of two major types. There are the physiological concomitants of emotional dysfunction, such as tension, fatigue, tachycardia, tension headaches, disturbances of gastrointestinal motility, and so on. With these symptoms the patient remains tense and anxious. A second group of symptoms are termed hysterical and are usually accompanied by some relief of anxiety. These symptoms include such things as paralysis, blindness, aphonia, cutaneous anesthesia, and the hysterical type of pain which may be localized to any area of the body. These symptoms that inhibit anxiety should be differentiated from similar symptoms or pains localized to specific areas of the body which are accompanied by anxiety.

The conflicts which cause functional disorders are always psychological, that is, within the psyche. It is useful for purposes of management to distinguish between conflicts in which the principle source of stress is predominately intrinsic or intrapsychic and those in which it is extrinsic or extrapsychic. Extrinsic sources of stress may be found in the interrelationships between the psyche and the soma, between the psyche and the social environment, or between the soma and the social environment. The chart illustrates this point.

In conflicts where the sources of stress are primarily intrinsic, the disturbance is usually deep and may reflect poor emotional adjustment in infancy, childhood, or adolescence. Persons in whom such situations exist often give a history of unhappy and disturbed childhood, long standing neurotic disturbances, frequent nervous breakdowns, multiple marriages, and other evidences of inadequate social and psychological adjustment. Occasionally symptoms are ascribable to a more recent and superficial intrapsychic disturbance, for example, anxiety or guilt relating to some unconfessed crime or misdeed.

The symptoms of intrinsic conflicts are usually more pronounced when the patient is alone and unoccupied. If the symptoms are of long duration and extend back to childhood, the disturbance is usually deep and intractable. If the symptoms are more recent, the conflict may be more superficial and lend itself to direct treatment.

Symptoms resulting from conflicts with extrinsic sources of stress are usually of more recent onset and are correlated in time of onset with the development of the conflict situation. They are more pronounced when the patient is in contact with the source of stress and tend to subside when he is alone and unoccupied. Fear of disease, real or imaginary, may cause functional symptoms, and derives from a disturbed relationship between the psyche and the soma. Marital problems, financial worry, and dissatisfaction with work or occupation exemplify disturbances of the interrelationship between the psyche and the social or environmental situation. The somatic environmental relationship may be disturbed in a patient who has been injured and fears that he will no longer be able to hold a job and earn a living. Often, as might be suspected, a single problem may involve psychological conflict with both intrinsic and extrinsic sources of stress.



The extrinsic sources of stress may be multiple. Logical management involves an evaluation of their respective roles.

Conflict situations are met by everyone every day. Normally a well-adjusted person resolves the conflict, avoids it, or makes some sort of healthy adjustment, and there are no symptoms. If the person fails to make a satisfactory adjustment and if his tolerance for stress is exceeded, functional symptoms will occur. Because of his symptoms the patient does not feel well and logically assumes that something is wrong with him physically. He consults a physician and recounts his somatic complaints. Only rarely does he, of his own volition, tell the physician of his anxiety and emotional problems.

RECOGNITION OF FUNCTIONAL DISORDERS

Diagnosis in patients with functional disorders requires identification of symptom complexes resulting from functional disorders and also from organic disease. The contribution of each to the total disability of the patient is estimated. The cause of the symptom complexes is sought. Physicians have long been taught to do this for organic disease. It is done also for functional disorders. Intelligent treatment is determined by an understanding of the cause of the difficulty. This applies equally to functional and to organic problems. Also, a diagnostic evaluation must include an estimation of the patient’s ability to understand, resolve, or endure psychological

conflict, with its accompanying tension and stress. An accurate diagnosis in these patients may be difficult indeed. Most physicians can recall patients whose troubles were considered "imaginary" but who turned out to have organic disease and others who had undergone extensive treatment for nonexistent "organic" disorders.

Identification of Organic and Functional Disease.—It has been said that if the physician will but sit and listen, almost every patient will give enough information to permit the correct diagnosis to be made or at least suspected. Good listening is particularly important for the physician who deals with functional problems. Symptoms are sought which suggest familiar complexes and syndromes. As the story progresses, questions are asked which are designed to complete a recognized pattern, functional or organic.

There is a group of symptoms which often result from long standing and unremitting emotional tension and strain. These are fatigue, "tired all the time," headaches, nervousness, exhaustion, and insomnia. The presence of one or more of these symptoms should alert the physician to the possibility that part of the problem is functional.

Other important symptoms are so-called anxiety symptoms. These conveniently may be thought of as manifestations of activity of the sympathetic nervous system. Many symptoms in this group occur together and may be said to constitute a sort of symptom complex. "Anxiety" symptoms are dizziness, "light headedness," nervousness, tremor, rapid heart rate, palpitation, numbness in the fingers and toes, difficulty getting a deep breath, "butterflies" in the stomach, occasional nausea and vomiting, constipation, diarrhea, and frequency of urination.

Finally, any unusual symptom or complaint may be the manifestation of a functional disorder. Hysterical symptoms belong in this group. Apparent anxiety and concern is usually diminished or even absent in hysterical patients. If an unusual symptom is present, which is accompanied by an unusually great amount of anxiety, there is often a special reason for the patient having the particular symptom. For instance, a person whose father died of angina pectoris may have an organically sound heart, yet have classical symptoms of angina pectoris as a manifestation of functional disorder. Situations of this sort may be extremely difficult to unravel. If the causative anxiety is overlooked, the patient's belief may be supported by his physician, with resulting additional disability.

Differentiation of "Organic" and "Functional" Symptoms.—Certain points may be used to differentiate a symptom of organic disease from a manifestation of a functional disturbance:

1. Of particular importance is the timing of its onset. Was the onset coincident with an emotional disturbance, or was there trauma, exposure to infection, or other cause?

2. It is useful to determine under what circumstances the symptom is intensified or relieved. Is the course that of a recognized organic condition or not? If the symptoms do not fit the pattern of any organic disease which comes to mind, a functional disturbance may be suspected. Such a suspicion is substantiated if the onset and

exacerbations and remissions can be correlated with emotionally disturbing events in the life of the patient. Such correlations are important and necessary if the symptoms are to be established as functional.

3. Supporting symptoms and signs must be considered. Do the ancillary complaints of the patient round out an organic or functional symptom complex?

4. It is valuable to note whether the patient has a normal emotional reaction to his symptoms. Either undue concern or an unusually apathetic attitude toward the complaint should suggest to the physician that he may be dealing with a functional problem.

5. An often helpful point is to determine whether this symptom awakens the patient at night. Functional symptoms seldom awaken a patient at night.

While taking a routine system review, the physician may conveniently round out the symptom complex. Particular attention is given to any symptom that does not seem to fit. It may be a clue to the correct diagnosis. For instance, a patient complaining of nervousness, easy fatigability, palpitations, weakness, and loss of weight may be suspected of having a functional disorder. This impression is strengthened if a history of emotional disturbance at the time of onset of symptoms is elicited. If, however, it is discovered that a patient's caloric intake was excessively high during this period of illness, this symptom will lead a physician to a correct diagnosis of mild hyperthyroidism.

Localization of Conflict.—If a functional disorder is suspected, a search must be conducted throughout the rest of the routine medical history to try to localize the causative conflict. Its nature and characteristics are important for planning effective and logical treatment.

How is a conflict located? Basically, evidence of tension, nervousness, or an unusual emotional response is sought. The routine medical history, including past history, family, marital, social, and occupational history, provides a framework for conducting the search.

Clinical Differentiation of "Intrinsic" and "Extrinsic" Stress Producing Situations.—Conflicts resulting from intrinsic or intrapsychic stress producing situations are identified primarily by their long duration, together with the timing of exacerbations and remissions of symptoms. In these instances symptoms often extend back to childhood or adolescence. There is often a long history of functional disability, punctuated by exacerbations of symptoms or by nervous breakdowns at times when the emotional load was increased. Unsatisfactory adjustment is often evidenced by multiple marriages, unstable work records, and so on. Such patients may have difficulty in getting to sleep, may sleep poorly and have nightmares. They are often fatigued and exhausted on arising in the morning. The symptoms improve when the person is occupied with some activity. These conflicts are usually deep, fixed, and of long duration, although they may occasionally be recent and superficial. Also, it is well to remember that extrinsic stress producing factors often accentuate the symptoms of a basically intrinsic disorder.

Extrinsic sources of stress or extrapsychic precipitating factors are frequent. The physician can help most of the patients in whom these are present. Thus, it is important to try to localize the extrinsic or extrapsychic

precipitating factors. These vary with the psychological, medical, sexual, religious, cultural, and economic background of the patient and his society. They differ in the rich and poor, the married and single, the young and old, the farmer, the factory worker, and the business executive. The physician is familiar with the background of his patient. Bearing these factors in mind and suspecting the presence of a functional disorder, he considers various applicable conflict situations while completing the medical history. Some of the common conflict situations are fear of disease, sexual and marital problems, conflicts with parents or "in-laws," financial difficulties, dissatisfaction with work or occupation, economic or social implications of physical disability, and religious conflicts.

Objective Signs of Tension.—Taking the family, marital, and social history provides an easy excuse for the physician to touch on potentially sensitive areas without arousing the antagonism of the patient. Objective signs of tension, such as a deep sigh, a blush, an involuntary clenching of the hands, or even the flicking of an eyelid, may indicate an emotional response. If these signs are noted, while the family history is being taken when reference is being made to the patient's mother, there is evidence of emotional tension in connection with the mother. It may signify fear resulting from the fact that the patient's mother died with similar symptoms, or it may mean that the mother is interfering in some way with the patient's life. It may be useful at this point to ask, "what sort of person is your mother, anyway?" A delay of an instant in answering, or perhaps an evasive answer, is evidence of emotional tension in this area. An unusually emotional response to any question is noteworthy. One patient, when asked a routine question about sexual adjustment, drew herself up defensively and emphatically stated, "I don't have any troubles with my sex life, Doctor." The physician may withdraw from this disturbing subject, but he is in possession of the information that all is not well with the patient's sexual adjustment. Such observations, made while scanning the probable or possible areas of mental conflict, provide the physician with much localizing information.

Subconscious Slips.—Surprisingly often, a patient makes a subconscious slip or an apparently unnecessary statement which gives important help in localizing a source of stress. It usually comes at an unexpected moment and is easily missed by the physician. One woman accidentally blurted, "My husband is no good," and then spent the next two or three minutes explaining how much he loved her and how good he was to her in every way. Another woman who was consulting many physicians, all of whom were trying to get at the root of her obscure complaints of disabling disease, suddenly exclaimed with a big smile, "You know, I get a big kick out of having all these doctors fussing over me." Another patient exclaimed repeatedly how she "adored" having her mother live with her and gave the impression that she must convince the physician also that this arrangement was satisfactory. Such clues, and they are surprisingly frequent, may give specific signs of the hidden and repressed emotional difficulty.

Some Important Questions.—If the physician is to be sure he is not overlooking the patient's real difficulty, several questions should be answered. He must know

exactly why the patient came to see him when he did. This is especially important when symptoms of long duration are present. The patient may have come because he knew someone with similar symptoms who recently died. If the physician knows this, and knows what the friend died of, he is then in a strong position to handle the problem. It is always wise to determine what disease the patient thinks he has. It is important to know this, first, because he may well have it, and, second, if he believes that he does, his anxiety cannot be relieved until he is convinced otherwise. It is often useful to ask the patient if he knows anyone else with similar symptoms. Sometimes this question will reveal the cause of the patient's anxiety. Usually it is well to ask the patient what he is afraid he might have. It is surprising how often this simple question will reveal a fear of cancer, high blood pressure, heart trouble, ulcer, syphilis, or insanity. Many patients will quite frankly reveal their fears when asked this question.

Emotional Release During Initial Interview.—Occasionally during the course of the interview, the patient will pour out his troubles to the physician with great relief of symptoms. The relief is most pronounced if an emotional release takes place. The patient in this way shares his trouble with someone else and is relieved of a part of the burden. This is not particularly frequent, however, and at times the physician will be faced with the problem of whether to try to get his patient to pour out his troubles. It has been well said that one must be careful not to remove the lid from the boiling caldron of the patient's emotions unless it can be got back on again. Probing into deep and complicated intrinsic psychological conflicts should be avoided by the general physician, unless he possesses adequate psychiatric training. The physician suspecting a problem involving guilt or shame may lose rapport with the patient by urging him to reveal himself, especially on the first visit. It has been established that the relationship between a male physician and a patient often falls into the psychological pattern of the relationship between the patient and his father. If the patient has a feeling of hostility or resentment toward his father, this attitude may be easily transferred to his physician. Often a situation of this kind may be detected by observation of the patient's emotional response to a mention of his father as the history is taken. If hostility toward the father figure exists, the male physician must be particularly careful not to antagonize the patient at the outset. In such cases a slow and careful approach is more productive in the long run.

If, however, the conflict is more superficial, particularly if there are obvious extrinsic precipitating factors, the physician may decide to try to get his patient to pour out his troubles. To accomplish this he may use an approach such as: "You seem to be the sort of person who gets upset easily. What sort of things upset you?" Or, more gently, "Is there anything you have noticed that really gets under your skin?" Such questions are often productive. If the localization of the conflict is suspected, the physician may say something like, "Whenever you speak of your mother, you seem nervous. What sort of person is your mother?" Or, "Your symptoms seem to be worse when you are working or soon after you get home. Is there something that gets under your skin at

the office?" In these instances positive and evasive answers are both significant.

When the area of the conflict is obscure, the patient may be told that, at times, symptoms such as his may be due to tension or stress, and he may be asked whether he is aware of any particular stress or strain or tension. Sometimes the patient will then discuss his emotional problems, perhaps with the statement that he does not see how this could possibly be causing his symptoms. Occasionally the physician may take advantage of what has been termed organ language. A patient may be nauseated because he "cannot stomach this or that." He may be asked if there is something that he has to put up with which he just cannot stomach. Similarly, a patient who complains of heaviness in his chest may have "something on his chest." Such techniques, in some instances, will provide the physician with the information he seeks.

In this way, then, while taking the history the physician is able to form some opinion (1) as to whether the primary difficulty is organic or functional and (2) if functional, whether the principal sources of stress are intrinsic or extrinsic. If they are extrinsic, he may gain some knowledge of the localization of some of the precipitating factors. Later, if the results of the complete physical examination and indicated laboratory procedures do not dispel the diagnostic impression, the physician sets the stage for treatment. Preparation for therapy, the technique of logical treatment based on the diagnostic evaluation and necessary follow-up, and prevention of recurrences will be the subject of another paper.

SUMMARY

The patient who comes to a physician is usually worried. Often the cause is obvious, and the anxiety is easily allayed. A large group of patients, however, do not have an obvious cause for their anxiety. These persons complain of nervousness, fatigue, tension, headaches, and a

variety of nervous and somatic symptoms. It is with this large group that this paper is concerned.

No single word or term has been generally accepted to designate the group of patients who are the subject of this discussion. It has been pointed out that all patients who have symptoms of nervousness have a disturbance of function as a whole. We have chosen to adhere to the term "functional" to describe this group of patients and their disorders.

Functional disorders are caused by psychological conflict. The sources of stress may be predominately intrinsic, that is, within the psyche itself, or they may be predominately extrinsic, that is, in the relationship between the mind and body, the mind and environment, or the body and environment.

The task of the physician is to determine in the time available how much of the patient's symptoms and disability is due to organic disease and how much is due to functional disorder. If a functional disorder is thought to be present, it is necessary to gain some idea of the underlying conflict situation.

The usual medical history, physical examination, and laboratory investigation may be used to detect the presence of functional disorders as well as organic disease. In the initial interview functional disorders should be considered equally with organic disease as a possible cause of the patient's symptoms and disability. Some symptom complexes of functional disorders have been discussed and outlined, together with the practical methods of distinction between the symptom of a functional disorder and the symptom of organic disease.

If a functional disorder is suspected, the physician should attempt to localize the underlying conflict situation. This is necessary for logical treatment. Simple techniques for identifying the probable conflict situation during the course of the routine medical history have been described.

909 Hyde St. (Dr. Watts).

SECRETARY OF THE BOARD

APOLOGIA PRO VITA SUA

Francis J. Braceland, M.D., Hartford, Conn.

and

David A. Boyd, M.D., Rochester, Minn.

When Gilbert and Sullivan, those astute observers of human foibles, wrote melodiously in "The Pirates of Penzance or The Slave of Duty":

Ah, when constabulary duty's to be done (to be done)
A policeman's lot is not a happy one

they might easily have substituted "secretarial duties" for constabulary duty and particularly have had in mind the secretaries of specialty boards—this even in face of the fact that their position in the social scale is well below that of constables. A cross between servant and

whipping boy, a board secretary might be compared in status with an umpire, except that he has much longer hours and gets no pay. If a team wins or a candidate passes his examination, it is because they are good or are well prepared and coached. If they lose or fail, *ipso facto* it is someone else's fault, and; in the case of board examinations, the board's fault, and, because he signs the paper, the secretary's fault. Thus in a relatively short time an obscure, peace loving physician becomes on a national scale what public officials sometimes call one another.

The board, and henceforth by this term we shall refer to the American Board of Psychiatry and Neurology, Inc., is praised occasionally, criticized sometimes, and

misunderstood frequently. To attempt to justify its existence or that of any of the medical boards would require a long, involved discussion and would not be appropriate here. Suffice it to say that if there were no "boards" something else would have had to be invented in place of them, for it is doubtful that present standards of specialty training could have been attained without the existence of standardizing and examining bodies. The purpose of this paper is not to defend the principles and philosophies that underlie the operations of boards in general, but rather to describe for the reader the situation as the secretaries see it. The attitude with which we undertake this discussion is one of respect and real affection for our colleagues, both those who give and those who take "the boards."

By way of introductory apologia several questions should first be discussed and dismissed, for the board is sometimes held responsible for things that are beyond its purview, alien to its philosophy, and outside its field of influence. In fact, the board is even more distressed about these things and protests them more frequently and more vehemently than do its critics, but with a corresponding lack of success. An example is the refusal of hospital privileges to capable practitioners of neurology and psychiatry because they do not hold board certificates as diplomates. This, in our opinion, is an unfair restriction, a form of unhealthy trade unionism, and a substitution of guild restriction for professional competence. The board objects strongly to this practice and will have none of it; but hospital administrators state blandly that local conditions frequently make it impossible for their lay boards of trustees to decide opposing professional claims and competence, and, as long as certification exists, they will use it as a convenient measuring rod, and thus the onus is passed on to the board. To explain to a physician who is unable to acquire or retain a position on a staff that this policy was neither originated nor approved of by the board is usually not a pleasant, easy, or successful task.

The utilization of certification to determine salary or job status is an equally unfortunate policy that is frowned on by the board, which has always refused to lend itself to such actions. Yet there are still some who are unconvinced that the board was not conceived and organized for the malign purpose of preventing them from receiving a 25% pay increase or a promotion. Patient and careful statements couched in conciliatory terms by the secretary are frequently unheeded by both victim and hospital alike, and the existence, usefulness, and value of the board are called into question, though it had nothing to do with the establishment of such policies.

Some states stipulate as a prerequisite for employment that the applicant must be a "diplomate or be eligible for examination." In this manner the board is unwittingly dragooned into the business of personnel screening. Applications for examination are received by the secretary, accepted in good faith, and the arduous task of investigation of the applicant's specialized medical training, experience, professional competence, and ethical standards is carried out. The applicant is found to be eligible and is invited to appear for examination, and then he blithely writes that he never intended to be examined but only

wished a statement of eligibility in order to secure a position in a state with this requirement. It is exasperating to learn that all this secretarial effort has been expended only for the purpose of job screening. By the same token, it is equally disturbing for an applicant to be denied an opportunity to work in a state because he is not "board eligible."

Physicians in general are not prone to suffer in silence. And who is the recipient of the firm and unequivocal statement of their feelings in these matters? The secretary of the board! This is due to the very human quality of reducing difficult problems to a person. It is not easy to wrestle with a "board," because of its fog-like quality of fragmenting and reassembling in different places and shapes. But the secretary is a different matter. Here is solid human flesh that remains in one place. Thus the secretary, not only as the mechanism of communication but as tangible evidence of the existence of the board, becomes the focal point in the turmoil. His function is to convey rulings, which are not always the desired ones, and to attempt explanation of situations as described above, and, needless to say, his communications are frequently unpopular.

As an example of the ire that may be directed at the secretary, let us consider the matter of certification on record, or the so-called Grandfather Clause. In earlier days it was possible to be certified on one's professional record, if certain requirements were met. It was determined that this policy would be discontinued Jan. 1, 1947, and that all further certification would be achieved only by successful examination. This decision was publicized for one full year and announced at all national meetings, in order to provide every opportunity for the dilatory to apply. Almost five years after the deadline applications are still received for certification on record, and no amount of tactful explanation can convince an applicant that he must stand examination. Instead, some of the applicants insist hotly that they have intended to apply ever since 1935 but never had the time, and, furthermore, ask us to send the certificate along by return mail without any more nonsense.

Additional repercussions of similar nature continued for years over a semantic question. When a diplomate achieves certification in one specialty, he may, by presentation of evidence of training and subsequent successful examination, achieve certification in the other field. The second examination and certification was called "complementary certification," because it completed his full certification in both neurology and psychiatry. Each published list of new certifications included those who had received such complementary certification. After the appearance of each list the secretary could expect a deluge of irate letters demanding to know why the board "complimented" those physicians with such certification while the writers were not "complimented" in the same friendly fashion. The secretary labored over long letters pointing out the different connotations of the words "complement," meaning complete, and "compliment," meaning courteous flattery. The years of phraseologic struggle took their toll, however, and, rather than face an eternity of long letters and labored explanations, we took the cowardly course. We changed the name to "supplemen-

tary certification," although this was not so satisfactory a designation but merely one less likely to cause trouble.

Contrary to general opinion, the preparation of applicants' credentials does not begin shortly before examination. Often the initial steps are taken during internship, when a prospective trainee writes to the secretary indicating his desire to undertake training primarily designed to make him a competent neurologist or psychiatrist or both and, incidentally, to fulfill board requirements at the same time. Often he wishes to have a program laid out in detail, even to the selection of the best training programs. To comply with his request would expose the secretary to the charge of favoritism, individual narrowness of approach, and undue domination and restriction of the broad sweep of individualized psychiatric training; furthermore, he would be suspected of an urge to standardize and mechanize the specialties. The secretary repeats the traditional board statement that there is no known best way to become a neurologist or psychiatrist and that it is recommended that the applicant follow his own bent and ideals, with board certification as a distinctly secondary goal. The secretary humbly refers inquirers to their own professors, to published lists of approved programs, to broad outlines of training programs, and to the American Medical Association Residency Information Service, with the result that the secretary is charged with being vague, indefinite, and unwilling to point out the one and only true way.

During the applicant's years of preparatory training the secretary is bombarded with letters requesting an unofficial evaluation of status. No matter how often it is emphasized that the physician's individual ideals of practice are the primary goal, applicants still write—sometimes it seems almost daily—to confer about changes in programs. Although the regulations are broad and inclusive, physicians still ask such questions as whether a year at a certain institution would be advisable and whether they should take certain courses. In spite of a prevalent belief that the board lives to regulate, the secretary constantly reiterates that the only sensible course to pursue is to prepare to be the best possible physician within the limits of one's ability and opportunities. Too frequently the return mail brings: "Thank you for your advice. Do you think I had better take a year at X?" And then we go over the whole problem again. There is no place for a short-tempered secretary, and, as the unfortunate incumbent of the office looks with exasperation at baskets full of letters, he must always remember that to each of these anxious correspondents his plans are a matter of crucial importance.

Meanwhile, formal applications arrive at the executive offices at the rate of 500 to 600 per year. Each one must be checked for completeness, and then all pertinent data extracted, typed, and forwarded to the American Medical Association for verification of claims of education, graduation, internship, professional and specialized training. The American Medical Association returns a check list, which is then compared with the candidate's claims. Simultaneously, reference forms are sent out to the sponsors whose names have been supplied by the candidate and to five other specialists in the field who are likely to have known the applicant during training or his years of practice.

An interesting commentary on the care with which physicians read board mail that they are about to sign is provided by the answers to the reference slips frequently received. The blue slips are for the references the candidate gives; the yellow ones are secret, and their issuance is unknown to the candidate. Although it is plainly printed on the yellow slips "this request is unknown to the candidate," often the addressee irately writes: "I cannot understand why this man ever gave my name as a reference." Sometimes they even telephone the candidate to tell him about this secret inquiry. The replies on these reference forms are often individual chapters in themselves. From one who has bitterly protested and has conducted a running internecine correspondence with the secretary about the board's insistence on his own personal fulfillment of requirements, we learn of our new applicant, "He is a good, competent, and ethical practitioner. Would suggest careful investigation, however, to learn if he has fulfilled all requirements." The same mail may contain such a reference and also a letter from the same informant suggesting that the requirements be modified, however, in the case of Dr. A, who, while he has not had the necessary basic training, is nevertheless an unusually fine and bright fellow. The sponsor knows the latter to be true because the applicant has been a close friend of his for several years.

By and large, however, physicians are honest and sincere, even with regard to their competitors. Often we hear, "I cannot stand him personally, but he is a well-trained, competent man." Since it is well known that the informant's confidence is never betrayed, the references are usually candid, even those of the sponsors whose names were supplied by applicants. Backbiting rarely if ever occurs, and, when it does, it is in minor issues, for almost all physicians rise above their own petty resentments in such important matters as certification. One instance was amusing, in that the references were so poor that more than 15 inquiries were sent out. Each reply was worse than the one preceding. By accident we finally struck on the applicant's analyst, and one could almost hear his gulp as he offered the dubious praise, "After two years of almost daily contact, I can honestly state that I am convinced that he is better now than he used to be."

Sometimes these inquiries inspire a vigorous chiding of the secretary: "I am sure that he has not had the required training, and I feel that you have been remiss in your investigations," and so forth. These are always answered, indicating the time and place of training and with a statement that the authenticity of such claims has been carefully checked. Almost always we receive an answer, both grudging and friendly, "I did not know Dr. M. had had that training. Anyway I am glad that you fellows are not asleep on the job." The friendly candor of the references is well demonstrated by one informant who said, "Please do not let Dr. Q take the examination now. He is not ready for it, and he will fail. He will then have to be as paranoid, defensive, and bitter as I was for years after taking and failing the examination because I was not ready." It was not easy, after such sincere assistance, to write to the informant and tell him that "on the record" Dr. Q had fulfilled the requirements and henceforth was the captain of his own destiny. For the mathematically minded it is interesting to note that with 600

applications per year and 8 inquiries per applicant, 4,800 pieces of mail are sent from and returned to this office, exclusive of all additional correspondence.

After the applications have been processed, passed on by the credentials committee, and the candidates notified, the actual task of setting up the examination is undertaken. The facilities of a large metropolitan center must be secured to supply adequate space and clinical material. For a large examination as many as 100 separate examining rooms are needed for basic and clinical psychiatry alone, plus an abundance of neurological material in addition, and it must be kept in mind that patients cannot tolerate repetitious neurological examinations. The board thus becomes deeply indebted and humbly grateful to those hospitals in which it has been a troublesome guest, because specialty neurological and psychiatric examinations completely disrupt hospital functions for a week or more. For the usual 300 candidates it is necessary to provide approximately 1,800 examining hours in two days, with care exercised so that no two assignments will be in conflict. It is also necessary to provide a rest period between examinations whenever possible. All this requires the assistance of about 110 examiners, who generously give up their practice and labor for the princely sum of \$10 per day.

Next the schedule must be dovetailed, so that each candidate is at the right place at the right hour and the right examiner is there to meet him at the time allotted. To avoid unnecessary waste and expense, such a schedule must be "airtight," and, therefore, there is little margin for error. However, at the last moment key examiners become ill, their wives go into labor, hospital investigations are instituted, railroad men strike, trains are late, airplanes are grounded, ad infinitum. It is then that the secretary becomes anxious and almost desperate.

Finally the examination gets under way. Candidates arrive in panic, and the secretary's first duty is to have a period of group psychotherapy. Ostensibly, this is a period of instruction on examination procedures, but really it is a "cooling off" period in order to permit the candidates to gain composure. Now the secretary begins his attempts at reassurance, usually by the simple method of pointing out that if the secretary could finally pass the examination, it is well within the capacity of any candidate. Then, however, his troubles really begin. Candidates forget to appear at the correct examining section, and frantic efforts then must be made to find a free period in an already tight schedule. Others have gone to the wrong hospital; or the taxicab driver has become lost, the candidate rushes in two hours late, and the schedule is torn apart again. One candidate arrived at the examination two hours late and was completely mystified about his tardiness. After frantic rescheduling, which permitted no further modification, he was missed at the next examination period. After a search of the grounds he was found reclining under a tree and, when questioned, explained in an astonished manner that he must have forgotten to set his watch ahead as he came across the country.

Individual psychotherapy must be undertaken with anxiety ridden candidates, discouraged ones reassured, baggage watched for late comers, and directions supplied

regarding the nearest drugstore, soft drink stand, telephone, coffee counter, and bathroom. Even more active medical first aid has been necessary for candidates who have fainted, and especially for one who revived his flagging courage too vigorously at a nearby bar. The latter wrote subsequently and indignantly demanded certification in those subjects that he had passed successfully before he became ill.

The secretary simultaneously acts as a runner between examining sections, collector and organizer of examination grades, and carrier of incoming messages. It is not unusual for him to search for half an hour for a candidate to deliver a telegram that almost invariably turns out to read, "Good luck to you, Joe, in your examination" and is signed "Mom." In the meantime, in some locations, preparations are under way with a caterer to serve luncheon to approximately 300 candidates and examiners, and this necessitates arrangements for the sale and collection of meal tickets.

At the end of each day of examination, the individual grades are presented to the board, and each candidate is carefully discussed and evaluated. The final notification form is prepared and mailed after midnight of the final day of examination. As the last notification is placed in the mailbox, the secretary usually collapses. As a matter of fact, after each examination one of us regularly took to his bed with exhaustion and acute upper respiratory tract infection.

There remains then only the matter of preparing diplomas and their mailing, preparation of lists of successful candidates for the journals and directories, explanations to indignant but unsuccessful candidates that they really did fail the examination and, no, they were not confused with someone of similar name, and then immediately beginning the plans and organization for the next examination. Accompanying the sigh of relief as the examination ends is the gloomy realization that in a few months the whole thing must be done again.

Among the many duties of the secretary is the formidable task of answering the assorted inquiries, which rival in scope and topic the "letters to the editor." For example, almost every mail includes a letter from an aspiring high school student: "I am writing a theme for my class in social studies. Please send all information on how to become a psychiatrist, the salary, education required, and the kind of work they do. P. S. My theme is due Thursday." Or, "Here are my dues for the American Psychiatric Association." We receive completed Federal questionnaires or even applications for jobs. Why these are sent to us is one of the world's greatest mysteries. Even more difficult to answer are the inquiries with the distinct paranoid odor: "My wife is being treated by Dr. X. Please send immediately all information about his training and professional standing." Or, "My son was in the state hospital for eight years with dementia precox. I removed him because he was not improving and put him under the care of Dr. Y. He recommends blank treatment. What do you recommend? P. S. Is he a good psychiatrist?"

It is not easy to remain tactful, imperturbable, and still answer such letters in a noncommittal manner. Those with forensic aspects are still more explosive. Attorneys have attempted to learn physician failed in

amination so that his testimony might be attacked, and we have received reams of testimony for comment. One paranoid hypomanic patient even sent a printed brochure of the court testimony in his suit against a psychiatrist for having placed him in a psychiatric hospital, suggesting that we take independent action against the physician and requesting advice for further legal action. Some of the requests are of such magnitude as to necessitate a week's secretarial work—for instance, "Please send me the names and addresses of all diplomates in Chicago and Los Angeles. I may be going to either town in the near future."

Some require nothing short of a miraculous divination: "We have an opening for a diplomate in neurology and psychiatry who can also do psychoanalysis. The salary for a man with proper qualifications is \$5,000 per year. Please send the names of half a dozen men who would be interested." The letters most likely to disturb the secretary are those that scold him for matters in which he has no jurisdiction or control: "Why are you not actively promoting psychiatric fellowships for physicians who speak Sanskrit? Are you anti-Sanskrit?" Or "My listing in the directory (which is published by a private printing house) is wrong. This is a serious matter to me and must be corrected at once, before I consult my attorney. I am at a loss to understand why your office does not exercise more care in these matters."

The secretary's job is not all bad, however, and frequently he is rewarded by a letter from a physician who really displays understanding. In our tenure of office we are glad to say we have only received three vitriolic and unfair letters. Our policy with these is to wait a while and then return them to the sender. They were written in heat and anger, and we know the candidates would not want them in their records. Also, we have been privileged to see a much better-equipped group of candidates come before the board as the training programs have taken hold. The men are avid, anxious, and under pressure, and the watchwords of the board are kindness, understanding, and patient but careful, thorough examination. Punitive action or harshness with candidates is not tolerated, and the men are treated as colleagues and fellow practitioners. The hope of the board is that the men will pass—they have met the standards, and, if it is justifiable, they are passed.

Scrupulous fairness is the policy used in grading the candidates at the board meeting at night, and often the discussion on individual men lasts a long time, since every facet of his examination and preparation is considered. We feel, as did the distinguished John Whitehorn, who, on leaving the board after having thrice been president, stated that his contact with the men who compose the board renewed his faith in human nature.

There remain other tasks within the province of the secretaryship. The functions of the board are primarily medical, and a close relationship is maintained with the Council on Medical Education and Hospitals of the American Medical Association, and there is active participation in the Advisory Board for Medical Specialties. Through these groups the American Board of Psychiatry and Neurology, Inc., remains in close contact with other specialty boards and with American medicine in gen-

eral. This includes the investigation and maintenance of standards in training programs and the preparation of long lists of hospitals in which approved training may be secured.

At this point in our jeremiad the reader must be wondering why anyone of average intelligence would involve himself in such a Laocoönian struggle. It cannot be on the basis of financial reward, because none of the directors receives a stipend. Some have implied the acceptance of the secretaryship is associated with a queer and as yet little known type of masochism. A different view was expressed by one applicant who requested and received a copy of the standard regulations and wrote in reply, "Dear Secretary: You are power mad!" If only he realized that our feelings at the end of each day are rivaled only by those of a clay duck in a shooting gallery that has safely completed another trip on his revolving, endless track!

What then is the motivation or at least the rationalization of all those, and particularly the harassed secretary, who are assigned the task of examining their colleagues? It is a belief that this is their contribution to the maintenance and elevation of standards of training and practice in their specialty and in medicine in general. Tremendous changes in training standards and professional preparation have occurred since 1934. As witness, in 1935 THE JOURNAL listed 16 training programs for neurology and 95 for neuropsychiatry. The Sept. 29, 1951, issue lists 79 for neurology and 243 for psychiatry. Since inception of the board in 1934, a total of 4,106 physicians have achieved certification in the specialties of psychiatry or neurology or both.

In the intervening time, extensive educational programs have been formulated and instituted, amalgamation of training facilities has been effected to supply all facets of experience, and courses have been charted that provide the trainee with some semblance of a plan of preparation. These are probably not the very best plans and certainly not the only ones, but now the tyro at least has certain guideposts. Secretaries are not as naïve as the flea on the chariot axle, who, on looking back, said proudly and compacently, "Lo, what a dust I have raised." The secretary knows that he has had the honor of serving a group that has made great efforts to raise standards in his particular specialty. In the expansion and improvement that has taken place a myriad of factors have played important roles, and among these we know that the American Board of Psychiatry and Neurology, Inc., has contributed its important part. In the light of these facts, it is well worth the worry, gloom, and travail that is now and always must be the destiny of the secretary of the board.

Tolerance.—Make it a rule never to be angry at anything a sick man says or does to you. Sickness often adds to the natural irritability of the temper. We are, therefore, to bear the reproaches of our patients with meekness and silence. It is folly to resent injuries at any time, but it is cowardice to resent an injury from a sick man, since, from his weakness and dependence upon us, he is unable to contend with us upon equal terms. —Benjamin Rush, M.D., *Medical Inquiries and Observations*, ed. 3, Philadelphia, 1809. Reprinted in *American Journal of Medicine*, November, 1951.

WEST FRANKFORT COAL MINE DISASTER

John E. Summers, M.D., West Frankfort, Ill.

At approximately 7:33 p. m., C. S. T., Dec. 21, 1951, an explosion occurred in the Orient no. 2 coal mine, owned by the Chicago, Wilmington & Franklin Coal Corporation, killing 119 men and hospitalizing 5 others. This was the worst mine disaster in the United States since 1928 and the second deadliest occurring in the Illinois coal mines. The worst coal mine disaster recorded occurred at Monongah, W. Va. in 1907, when 361 men were killed.

THE MINE

The Orient no. 2 coal mine is located 3 miles northwest of West Frankfort, Ill., and 70 miles southeast of St. Louis. The mine was opened 29 years ago and is the largest shaft coal mine in the world, with a daily output of 9,500 tons of coal. It holds a world record for coal mined during an eight hour shift, 15,152 tons. The mine covers an area of 12 square miles and is approximately 550 ft. below the surface. There are four shafts, two of which are used for mining operations. The other two shafts provide ventilation and contain stairs that are used for emergency exits. The main shaft is known as no. 4.

EXPLOSION

Coal mine explosions are due to the ignition of methane gas and/or of the coal dust in the air of the tunnels. This explosion occurred in the north part of the mine and was not felt in other parts of the mine or on the surface. The force of the blast is demonstrated by an 8 ton piece of machinery that was knocked off its rails. Heavy steel rails were torn from their tracks and twisted in various forms. Supporting timbers were knocked down and cave-ins were precipitated. It is estimated that about 15 men were working in the immediate area of the explosion. The bodies of these men were mutilated so that identification was very difficult. Old operative scars, teeth and dentures, and finger printing were resorted to to identify the bodies.

When the concentration of methane and oxygen reaches combustible proportions, a spark or flames ignite the methane, resulting in an explosion of tremendous force. When fine particles of coal dust are in the air, a coal dust explosion is then propagated. Carbon monoxide is produced by the combustion of methane.

The U. S. Bureau of Mines inspectors have listed the conditions responsible for the explosion¹:

1. An inadequate ventilating system in which air that ventilates the working sections of the mine first passes open approaches to abandoned and caving areas which contain explosive gas. No provision had been made at the time of the disaster to keep abandoned areas free from accumulations of explosive gas.
2. The operation of nonpermissible electrical equipment which is capable of igniting gas.
3. The presence of large accumulations of fine coal dust of an explosive nature created by mining operations. This coal dust, principally along roadways, was not removed from the mine or rendered inert by the application of sufficient rock dust.

Injuries result from: (1) the blast force, (2) the flash-fire, (3) carbon monoxide poisoning, and (4) falling timbers, rocks, and machinery.

It is unfortunate that more accurate studies into the causes of death from the explosion were not made. It is probable that a large percentage of the victims succumbed to carbon monoxide poisoning. The rapidity of diffusion of carbon monoxide after the explosion is evidenced by the dead birds found lying on the floor of the no. 4 shaft elevator a few minutes after the explosion, which occurred about two miles away.

RESCUE OPERATIONS

A few minutes after the explosion dense black smoke was seen billowing from shaft no. 4. The coal company surgeons, Drs. A. F. Barnett and C. H. Williams, were called to the shaft and helped to organize the rescue operations. Trained rescue workers were summoned. Over 500 men took part in this task, which lasted for three days. Twenty rescue teams, each consisting of six men, worked in relays. The advance rescue men wore asbestos fire fighting clothing and gas masks equipped with oxygen tanks, in addition to the regulation helmeted lamps and battery strapped around the waist. All electric current in the mine was shut off. The bodies of the

Major Mine Disasters in Illinois

Place	Date	No. Killed
Braidwood.....	Feb. 16, 1883	69
Zeigler.....	April 13, 1905	49
Zeigler.....	Jan. 10, 1909	26
Cherry.....	Nov. 13, 1909	259
Royalton.....	Oct. 27, 1914	52
Royalton.....	Sept. 28, 1918	21
Johnston City.....	Jan. 25, 1924	33
West Frankfort.....	Jan. 9, 1928	21
Moweaqua.....	Dec. 23, 1932	54
Centralla.....	March 25, 1947	111
West Frankfort.....	July 24, 1947	27

victims were carried on stretchers, with head lamps providing the only illumination. Those miners considered dead were left while the rescuers pushed ahead to reach those who might be alive. As the victims were located from two to four miles from the shaft, the rescue was hampered, not only by gas, cave-ins, and obstructing timbers and machinery, but also by the long distances over which the stretcher bearers had to walk.

The few survivors, after being brought to the surface, were given oxygen and brought to the hospital. Numerous rescue workers required treatment at the mine, and three were hospitalized for short periods. The dead were carried to a temporary morgue located in the gymnasium of the West Frankfort Central Elementary School. Aid to the rescue workers at the mine, the morgue, and elsewhere was systematically and efficiently rendered by the Salvation Army and the local Red Cross.

Chief Surgeon, U. M. W. of A. Union Hospital.

Drs. Owen H. Taylor and Charles E. Ahlm assisted in the emergency care of the hospitalized patients.

1. Final Report on Major Explosion Disaster, Orient No. 2 Mine, Chicago, Wilmington & Franklin Coal Company, West Frankfort, Franklin County, Illinois, United States Department of the Interior, Bureau of Mines, Region 8, 1951.

PREPARATIONS AT HOSPITAL FOR WOUNDED

As soon as the report of the explosion had been made public, the hospital authorities began preparations to receive an unknown number of seriously injured men. All patients in the hospital who were able to be moved were forewarned of that possibility. Requests for blood plasma were sent out to outlying hospitals, and technicians were called in from surrounding towns to assist in necessary laboratory work and blood typing. Additional oxygen therapy apparatus was secured, and blood donors were called for. Twenty-five pints of blood, type O and A, were rapidly collected. In emergencies we have been quite successful in using type O blood, to which has been added blood group specific substances A and B.

REPORT OF CASES

CASE 1.—At approximately 8:30 p. m., Dec. 21, 1951, the first patient, a white man, 53, was brought to the hospital. His main complaints were nausea, vomiting, and headache. He had



Fig. 1.—Coal company surgeons (left background) watch as rescuers bring one of the survivors from the shaft of the mine.

been working in the periphery of the explosion area and was suffering from carbon monoxide poisoning. This man's job served as a "nerve center" for the explosion area, since he kept in constant contact with all parts of the mine by means of telephone. The first knowledge of the explosion occurred at 7:33 p. m., C. S. T., Dec. 21, 1951, when the patient experienced a sensation as if someone had suddenly clapped both hands over his ears. Shortly thereafter he felt a terrific wind, described as "a tornado" coming from the tunnel. He attempted, with another miner, to shut the steel safety doors leading to the mine shaft but was unable to do so because the doors had been blocked open with various mine equipment. He then rushed toward the mine shaft to escape and lost consciousness as he fell near the elevator. He was pulled onto the elevator and was brought to the surface by two other coal miners. Prior to losing consciousness he noted that there were dead birds lying on the elevator floor. These birds had been roosting above the elevator shaft in the warm air and had been overcome by the carbon monoxide fumes. Physical findings were essentially normal, except that the patient's skin and mucous membranes appeared pinker than normal. During his hospital stay he complained of nausea, vomiting, headaches, and nervousness, but he improved rapidly and

was discharged at 10 a. m. on Dec. 24, 1951. Daily follow-up studies revealed continual improvement, but the patient still complained of attacks of nausea and vomiting, usually coming on in the afternoon. He also complained of inability to sleep at night.

CASE 2.—A white man, 33, was admitted to the hospital at 10:30 p. m., Dec. 21, 1951. He was admitted in a semicomatose condition and was unable to give any satisfactory history. He had previously been treated in the hospital in 1950, at which time a vagotomy had been performed for a chronic, intractable, duodenal ulcer. This operation had been successful, as measured by follow-up studies and roentgenograms that had been last reported as showing a normal intestinal tract. On examination the patient moaned and responded to painful stimuli. He was covered with smoke and coal dust, so that his features were not at first recognizable. There were first and second degree burns of the hands, upper extremities, neck, face, and scalp. The eyelids were reddened, and the conjunctivas were markedly inflamed and swollen. The temperature was 99 F, the blood pressure 130/70, the respiration rate 24, and the pulse rate 90. The rest of the physical findings were essentially normal. There was no evidence of pulmonary congestion at this time. The patient was very thirsty and moaned for water repeatedly. Water was given to him, and there was no vomiting. He was placed in an oxygen tent. Plasma, and later, whole blood was given intravenously. The initial dose of $\frac{1}{4}$ grain (15 mg.) of morphine was not adequate, and a second dose was required. Subsequently meperidine



Fig. 2.—A survivor, taken out of the mine shortly after the explosion, being carried to a waiting ambulance by trained rescuers wearing 40 lb. (18.1 kg.) oxygen breathing apparatus with the battery strapped around the waist.

(demerol®) hydrochloride was used instead of morphine. Antibiotics and tetanus antitoxin were administered. Frequent determinations of the pulse, respirations, and blood pressure were recorded. Laboratory studies on Dec. 22, 1951, showed the red blood cell count to be 5,360,000, the hemoglobin 14.05 gm., and the white blood cell count 11,500. Urinalysis was normal with a specific gravity of 1.020. Blood determination for carbon monoxide saturation was taken at 2 p. m. on Dec. 24, 1951, and was reported as showing a 40% to 50% blood saturation. Carbon monoxide saturation on Dec. 26, 1951, was reported as being less than 5%. He began to clear mentally on Dec. 24, 1951, and was able to answer questions on Dec. 25, 1951. At this time he had no recollection of the explosion. The last thing that he remembered was that he had been working down in the coal mine. At the present time the patient is much improved.

CASE 3.—A white coal miner, 47, was admitted at 1:40 a. m., Dec. 22, 1951. The patient was unconscious and appeared to be desperately ill. The skin was cold and cyanotic. The head was rigidly held in hyperextension. The eyeballs were fixed and directed upward and to the right. Generalized clonic convulsions occurred intermittently, and the jaws were held tightly together. The blood pressure was 90/60, the pulse rate 100, the respirations 30 per minute and stertorous. There were no external evidences of injury. He was placed in an oxygen tent, and 2 pt. (1,000 cc.) of plasma and 3 pt. (1,500 cc.) of whole blood were administered before the patient had recovered from the initial shock. Broncho-

scopic examination was done initially, and large amounts of blood-tinged fluid were obtained from the trachea and bronchi. Repeated laryngoscopic examinations and direct tracheal aspirations were required because of the continued accumulation of fluid in the trachea. These operations were somewhat hampered owing to the spasm of the jaw muscles. There was a short period of improvement in the vital signs, but the patient remained comatose throughout. Portable chest roentgenograms were taken on the afternoon of Dec. 22, 1951, and showed patchy consolidation throughout both lung fields. Pulsus alternans was noted, and rapid digitalization by parenteral administration was performed. Fluids (5% dextrose in water) were given intravenously, and all the urinary output was collected through an indwelling urinary bladder catheter. Antibiotics were administered in large doses. The urine output for the first 24 hours was 1,200 cc.; for the next 24 hours, the urine output was 955 cc. Owing to the necessity for repeated tracheal aspirations to remove the fluid from the trachea and bronchi, a tracheotomy was performed at 2 p. m. on Dec. 23, 1951. The patient continued to experience cyanotic attacks of progressive severity, the pulsus alternans continued, and respiratory arrest occurred at 8 p. m. on Dec. 23, 1951. Stimulants and artificial respiration were administered but were of no avail. The heart continued to beat for approximately 8 minutes after the respirations ceased. Laboratory studies on Dec. 22, 1951, showed the red blood cell count to be 5,200,000, the hemoglobin 15.05 gm., and the white blood cell count 17,000. Urinalysis findings were essentially normal; the specific gravity was not determined at this time. Permission for autopsy was refused by the family.

While no blood determinations for carbon monoxide saturation were performed, it is believed that this patient died from carbon monoxide poisoning. After the initial shock it was noted that the skin and mucous membranes appeared much redder than normal, and the venous blood was cherry red. The clinical signs indicated severe damage had occurred to the central nervous system.

CASE 4.—A white man, 54, was admitted at 1:40 a. m., Dec. 22, 1951. This coal miner had been working with the patient in case 3. Examination showed that he was disoriented and restless. He, like the others, was blackened with coal and smoke. There was a short laceration of the skin in the left frontal region. Superficial burns were noted on the left side of the face and about the left ear. The lids were reddened, and the conjunctivas were edematous and congested. There were no other external evidences of injury of any significance. The mucous membranes appeared redder than normal. The blood pressure was 140/80, the pulse rate 90, and the respirations 26 per minute. The patient was placed in an oxygen tent. Whole blood transfusions were started. An indwelling catheter was placed in the urinary bladder. Antibiotics and tetanus antitoxin were administered. Fluids were given intravenously. The urinary output of 1,000 cc. per day was maintained. The patient was very restless and nauseated but was able to cough up abundant mucus from the trachea. He remained confused, unable to answer questions. He had no recollection as to time, place, or persons, until Dec. 25, 1951, when he appeared to recognize certain members of his family. On Dec. 26, 1951, he began to ask questions but still had loss of memory for present and recent happenings. He continued to improve slowly, mentally, but has no recollection of the explosion. Laboratory studies on Dec. 22, 1951, showed the red blood cell count to be 4,960,000, the hemoglobin 15.05 gm., and the white blood cell count 18,700. Urinalysis findings were normal, with a specific gravity of 1.003. On Dec. 24, 1951, the red blood cell count was 5,310,000, the white blood cell count 12,300, and the hemoglobin 14.05 gm. Urinalysis showed a specific gravity of 1.017, 1+ for albumin, 5 to 7 white blood cells, and 15 to 25 red blood cells. Blood taken at 2 p. m., Dec. 24, 1951, was reported as showing a 40% to 50% carbon monoxide saturation. Blood taken on Dec. 26, 1951, was reported as showing a carbon monoxide saturation of less than 5%. At the present time the patient is greatly improved, and his memory for past and recent events is practically restored.

CASE 5.—A white coal miner, 44, was admitted on Dec. 24, 1951, at 6:45 a. m. When the rescuing party found this coal miner, they had removed 106 dead bodies from the coal mine,

and all hope for any survivors had long vanished. This coal miner had been working with nine others in the periphery of the blast area at the time of the explosion. The blast had knocked the men down, but they had recovered and had attempted to escape from the gas (carbon monoxide) that followed the explosion. Their exit to the mine shaft had been cut off by the carbon monoxide, and they attempted to secure themselves a place in the rocks, as high as possible, away from the approaching gas. They erected a barricade (called a brattice) consisting of burlap cloths, which was supposed to divert the gas from the place of refuge; however, the gas seeped in, and shortly thereafter the victims were overcome. The lone survivor of this group of 10 men was rescued 57½ hours after the explosion. Prior to losing consciousness he wrote a short note on the back of a cough drop box (the use of various types of cough drops is very prevalent among miners). The note read, "May the good Lord bless and keep you, dear wife and kids. Will meet you in heaven. Your husband and dad, Cecil." The patient was conscious when the rescuers reached him, and he has remained so. Examination revealed no evidence of external injury except for two small contusions in the right lumbar region. He complained of being very weak and thirsty. He was placed in an oxygen tent. Fluids were given, orally and intravenously, and whole blood administered. On admission the temperature was 99 F, the pulse rate 80, the respiration rate 22, and the blood pressure 100/60. The skin was abnormally pink, as were the mucous membranes. At 6:30 a. m., Dec. 25, 1951, the blood pressure fell to 80/50 with no other change in the vital signs. At this time the patient also complained of a headache. Blood transfusions were administered, and improvement resulted. During the first 24 hours of hospitalization, the patient was able to drink water and requested coffee on Dec. 25, 1951. Thereafter he was able to take food by mouth. The temperature rose to 101 F on Dec. 25, 1951, and to 102.6 F on Dec. 26, 1951. Large amounts of antibiotics had been administered since admission. On Dec. 27, 1951, the temperature reached a maximum of 101 F, and the patient complained of pain in the right lower chest region. The temperature has returned to normal, and the chest signs of pneumonitis in the right lower lobe have subsided. Progress is excellent at the present time. Laboratory studies on Dec. 24, 1951 showed the red blood cell count to be 5,000,000, the white blood cell count 9,050, and the hemoglobin 16.45 gm. Urinalysis findings were essentially normal, with a specific gravity of 1.016. All urine was collected through an indwelling catheter for the first two days of hospitalization. Blood taken on Dec. 24, 1951, at 2 p. m. for carbon monoxide determination showed a saturation of less than 3%. Blood taken for carbon monoxide determination on Dec. 26, 1951, showed no carbon monoxide in the blood.

This patient apparently suffered carbon monoxide poisoning, dehydration, and starvation. After the carbon monoxide was liberated by the oxygen therapy and the dehydration was corrected, he improved rapidly. He had one episode indicative of beginning vascular collapse after admission, and pneumonitis, which has responded to treatment, also developed in the right lower lung. At the present time his condition is improved, and full recovery is expected. He still complains of severe headaches, nervousness, and inability to sleep.

SUMMARY

At 7:33 p. m., C. S. T., Dec. 21, 1951, an explosion occurred in the coal mine Orient no. 2, in West Frankfort, Ill., killing 119 men. The deaths were due to (1) the blast force, (2) carbon monoxide poisoning, (3) the flash-fire, and (4) falling objects. It is recommended that should another such disaster occur, pathologists be called and autopsies performed in order to ascertain the causes of death. The determination of carbon monoxide saturation of the blood would be extremely helpful. It is my opinion that a larger percentage of the men were killed by carbon monoxide poisoning than is generally known.

2. Dr. R. M. Johnson went down into the mine to assist in this patient's rescue.

POLLEN PREVALENCE AND POLLEN-FREE AREAS

Oren C. Durham, North Chicago, Ill.

The essential objective in atmospheric pollen research is to learn how much of what kinds of allergenic pollen are likely to be inhaled by sensitized persons at any time and in any locality. This objective may be amplified in further detail as follows: (1) to assist in the clinical evaluation, locally and generally, of known allergenic pollens, (2) to discover, identify, and help to evaluate new allergenic pollens, (3) to clarify the role of meteorologic, topographic, and other local factors affecting pollen prevalence and pollen dispersal, and (4) to find areas where, as a result of natural advantages or control measures, or both, the air is relatively or entirely free from pollens of particular species. Obviously, air analysis furnishes an excellent yardstick by which to judge the anti-allergenic value of weed eradication campaigns and to test the truth of advertised claims for pollen-free vacation resorts.

At present all routine sampling of air-borne allergens is done by the gravity method, in which all pollen grains and other atmospheric debris are allowed to fall on a petrolatum (vaseline®) coated slide for a period of 24 hours. The pollens found on a unit area (1 sq. cm.) of the slide are then identified and those of each species or allergenically related group counted separately. Finally, the resulting square centimeter figures for each kind of pollen may be converted to approximate cubic yard equivalents by factors which have been worked out by extensive laboratory and outdoor experiments. The present standard technic includes the use of a special exposure device and the choice of the place of exposure—usually the top of a tall building in the business section of the city. This technic, as recommended in 1945 by the Pollen Survey Committee of the Council on Aeroallergens of the American Academy of Allergy,¹ has met with the wide acceptance by allergists, aerobiologists, and public health officials throughout the United States, Canada, and foreign countries. Current statistics are being reported to the Pollen Survey Committee each year from nearly 200 communities (see typical report of monthly pollen totals for Washington, D. C., for 1950, Table 1).

RAGWEED POLLEN

The clinical usefulness of daily ragweed pollen records is emphasized by the Chicago figures for 1949 and 1950 (Fig. 1). For nine consecutive days during late August and early September, 1949, the ragweed pollen concentration remained at a very high level—400 to 500 pollen grains per cubic yard of air. If, during that period, the results in treatment of local cases of hay fever were not perfect, everyone could be sure of the explanation. In 1950 it was just as important to know why pollen treat-

ment and supplementary medication during the same part of the season seemed unusually effective. Instead of abnormally high concentrations as in 1949, the figures for the 1950 season fell to all-time low levels, not only for those same nine days but for the remainder of the season as well. In seeking an explanation for the shortage of wind-blown pollen after Aug. 26, 1950, it was first noted that the short and giant ragweed crops were as luxuriant as usual. But weather records showed that except for one day in four weeks the wind had blown continuously from the north sector. In Chicago cool north winds always retard pollen production or discourage pollen distribution, or both. It is pertinent to add that the three days of low concentration in early September, 1949, were also caused by north winds.

TABLE 1.—Pollen Record for Washington, D. C., 1950*†

	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sep.	Oct.	Total
Maple.....	5	15	18	155	387	4	...	...	...	...	592
Alder.....	11	45	6	...	...	...	...	...	...	...	62
Elm.....	3	51	410	20	2	...	...	...	...	...	516
Juniper.....	8	17	63	5	...	...	...	...	...	...	93
Birch.....	..	2	12	142	224	6	...	...	...	...	336
Sycamore.....	..	...	3	95	265	21	...	...	...	...	384
Poplar.....	..	...	6	27	...	...	...	...	...	...	33
Oak.....	..	...	2	175	960	7	...	...	...	...	1,144
Willow.....	..	...	...	40	2	...	...	...	...	...	42
Sweet gum.....	..	...	...	25	36	...	...	...	...	...	61
Ash.....	..	...	...	23	17	...	...	...	...	...	40
Beech.....	..	...	...	14	11	...	...	...	...	...	25
Linden.....	..	...	...	8	56	46	2	...	...	...	112
Red mulberry..	..	...	...	84	153	90	...	...	...	...	327
Paper mulberry	..	...	...	...	57	...	...	3	3	...	63
Walnut.....	..	...	...	...	3	3	...	...	...	...	6
Hickory.....	..	...	...	...	25	...	...	...	...	...	25
Tree of Heaven	..	...	...	...	...	124	...	...	...	...	124
Grass.....	..	...	...	4	76	200	60	31	46	5	422
Red sorrel.....	..	...	...	...	122	92	...	...	...	...	214
English plantain.....	..	...	...	...	13	115	62	13	2	...	205
Goosefoot and amaranth.....	..	...	...	...	...	...	...	10	16	...	26
Composite.....	..	...	...	...	...	2	18	3	6	3	32
Ragweed.....	..	...	...	...	...	...	...	354	1,122	14	1,490
Miscellaneous..	38	20	52	164	134	58	38	14	12	3	533

* These figures indicate accumulated monthly and annual totals of daily average cubic yard content.
† Data from Dr. Eloise W. Kailin.

Data on the time of onset, apex, and termination of the ragweed season in many different localities are necessary in comparing the skin reactions and histories of pollen-sensitive persons who have resided in more than one area. Through extensive routine aerobiologic studies it has been shown, for example, that the ragweed hay fever season is appreciably later at Little Rock than at Winnipeg or Chicago, while at Houston the apex of pollination occurs more than a month later than in the North, and that the season is consistently longer in the South than in the North. In the southern half of Florida mild to moderate exposure is possible over a period of six months, due to pollen from a locally adapted strain of short ragweed which comes through the ground in the fall, grows all winter and reaches anthesis in May or June. In Arizona and southern California there are two distinct ragweed seasons each year—spring and fall—caused by two different types of false ragweed (Franseria).

Read in the Session on Allergy before the Section on Miscellaneous Topics at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 13, 1951.
Chairman, Pollen Survey Committee, Council on Aeroallergens of the American Academy of Allergy; Chief Botanist, Abbott Laboratories; Assistant Professor, Lecturer in Allergy, Department of Medicine, College of Medicine, University of Illinois.
1. Durham, O. C., and others: Report of the National Pollen Survey Committee of the American Academy of Allergy on a Conversion Factor for Gravity Slide Counts, J. Allergy 18: 284 (July) 1947.

Ragweed pollen incidence on a continent-wide scale is shown on the map (Fig. 2), where the comparative areas of the 200 discs indicate the comparative accumulated totals of ragweed and sagebrush pollen caught on a square centimeter of slide area in each place in a whole season. More than 250 other communities have been studied and could have been plotted if there had been room on the map. In most of these the air testing has been carried on for several seasons, some for as long as 20 years, so the plotted data are average totals. In the area between the Rocky Mountains and the Eastern seaboard, the abundance of ragweed pollen is truly astonishing. The breadbasket of America, where almost every wheat field is also a ragweed field, is a veritable Pandora's pollen box. Here strong daytime thermal currents and unobstructed prevailing westerly winds sweep up and suspend uncounted tons of pollen in clouds of varying density, often reaching heights of more than a mile above ground. The map serves to locate the ragweed pollen-free areas, as well as the heavily contaminated zones. The pollen-free and nearly free areas are indicated by two easily recog-

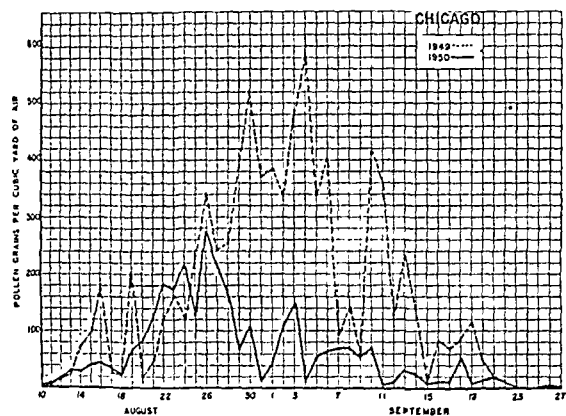


Fig. 1.—Ragweed pollen incidence in Chicago (data from Drs. T. B. Bernstein, William Grater, and T. B. Dannenberg).

nized symbols. A list of all places ² with excellent ragweed records is given in Table 2.

Alaska, western British Columbia, western Washington and Oregon, as well as many parts of California, including all the national parks of the Pacific states, have excellent ragweed ratings, although limited local exposure is possible in most of the cultivated areas of central and southern California. These low figures of the West Coast do not mean that all ragweed sufferers of the middle states will be permanently cured of inhalant allergy by moving to the West Coast, for some of these middle-states sufferers are sensitized to other pollens than ragweed or have the capacity to pick up readily sensitivity to new types of pollen.

Conditions range from fair to very good in the higher parts of the Rocky Mountains and intermountain states, including the national parks of the region. Very little trouble has been experienced by ragweed-sensitive tourists at Yellowstone except when they tramp in the sagebrush. In most of western Canada ragweed pollen concentrations are light. Even at Winnipeg very little ragweed pollen appears on the test slides except when strong winds blow from the Red River Valley across the border along the Minnesota-North Dakota line.

The upper Michigan peninsula has the double advantage of heavy woods and a growing season which is too short and too cool for maximum ragweed development, but in many instances these advantages are offset by the prevailing westerly winds and the rhythmic recurrence of strong south winds carrying pollen from Minnesota, Wisconsin, and lower Michigan. In the populous districts of southern Ontario and Quebec ragweeds are abundant, so one must go to the mountainous regions adjacent to northern New Hampshire and Maine or beyond the city of Quebec into the Gaspé country to find a satisfactory degree of relief. Excellent coordinated atmospheric pollen studies are being carried on in Ontario, Quebec, and in all the maritime provinces.³ While common ragweed is known to have invaded the Annapolis

TABLE 2.—Places with Perfect or Extremely Low Ragweed Records

United States and Alaska

Alaska: Fairbanks, Juneau, Nome
 Arizona: Phoenix, Grand Canyon National Park
 California: El Centro, Escondido, Lassen Volcanic National Park, Los Angeles, Monterey, Oakland, Pasadena, Sacramento, San Diego, San Francisco, Sequoia National Park, Yosemite National Park
 Colorado: Glenwood Springs, Mesa Verde National Park, Pikes Peak, Rocky Mountain National Park
 Florida: Fort Myers, Key West, Miami Beach
 Idaho: Moscow, Sun Valley
 Maine: Houlton, Newagen, New Portland, Presque Isle, St. Francis
 Montana: Glacier National Park, West Yellowstone
 Nevada: Reno
 New Hampshire: Colebrook, Errol, Lancaster, Moosilauke
 New York: Blue Mountain Lake, Keene Valley
 Oregon: Portland, Crater Lake National Park
 Utah: Bryce Canyon National Park, Zion National Park
 Washington: Mt. Rainier National Park, Olympic National Park, Seattle
 Wyoming: Grand Teton National Park, Yellowstone National Park

Canada

Manitoba: Russell, The Pas
 New Brunswick: Bathurst, Fredericton
 Newfoundland: St. John's
 Nova Scotia: Cape Breton Highlands National Park, Ingonish Island
 Prince Edward Island: Prince Edward Island National Park
 Quebec: Chandler, Father Point, Gaspé, Grand Rivière, Îles-de-la-Madeleine, Matapédia, Mont-Albert, Gaspésie, Mont Joli
 Saskatchewan: Prince Albert

Cuba

Havana

Bermuda

Hamilton

Valley of Nova Scotia, most of this province is probably still quite free of the weeds, as are New Brunswick, Prince Edward Island, and Newfoundland.

Pollen research has been carried on for a number of years during the fall season in about 50 cities and towns in the Catskill and Adirondack Mountains of New York by the State Department of Health.⁴ Likewise, in the White Mountains of New Hampshire the State Department of Health has studied some 36 communities.⁵ Throughout the state of Maine 25 test stations are serviced from the laboratories of the University of Maine.⁶ Many fairly good ragweed refuges and a few very good

2. Durham, O. C., and others: Report of the Pollen Survey Committee, 1950, unpublished data.

3. Campagna, E.: Ragweed Pollen Survey in Quebec for 1949, read before the Third Meeting, Eastern Section, National Weed Committee, Jan. 30-31 and Feb. 1, 1950, Ottawa, Canada. Unpublished data.

4. Gilcreas, F. W.: Unpublished data.

5. Vintinner, F. J.: Ragweed Free Areas in New Hampshire, New Hampshire State Department of Health, Division of Industrial Concord, N. H., May, 1950.

6. Vickers, M. A.: Unpublished data.

ones have been discovered in the mountain parts of these three states, but constant care must be exercised in evaluating the annual records from these areas. Even though a community is once proved to be virtually pollen free, there is no guarantee that it will remain so. Careful spraying of roadsides by highway authorities, combined with organized ragweed destruction in a given community, is sometimes highly effective if the community is surrounded by plenty of wooded country. But when this insulation is insufficient or the vigilance of the state authorities or the citizens is relaxed, a good record of one season may often be followed by a very poor one.

Except at Miami Beach, the possibility of ragweed refuges in Florida has received comparatively little attention until the 1950 season, when the state board of health instituted a statewide survey.⁷ Ragweeds flourish in the cultivated farm and orchard lands of northern and central Florida, as well as in the rich glade soil of the southern part of the state. But, fortunately, they cannot compete successfully with the native tropical vegetation. Where tilled soil is neglected, it produces ragweed for only one season, after which it is taken over by more vigorous plants. Large areas in southern Florida are given over completely to grasses or sedges. It will be seen from the map (Fig. 2) that, except for Sebring, all the better ragweed records are from points on or near the coast, even as far around the Gulf Coast as Pensacola.

On the subject of ragweed control, it is pertinent to remark that neither legislation nor community efforts directed toward this end in the central agricultural states can be taken seriously. To promise the effective suppression of air-borne ragweed pollen in either a local community or a whole state in this part of the country is equally absurd.

RAGWEED-RELATED SPECIES

The national aerial distribution of pollen of sagebrush (*Artemisia tridentata*) and other *Artemisia* species is shown on the same map with the ragweeds because most persons who are skin sensitive to ragweed are also equally skin sensitive to any or all of the sages, even in areas where the latter are absent. A glance at the map (Fig. 2) will show that in only a few places in the plateau states, Sun Valley, for example, do sagebrush pollen concentrations exceed those of the local ragweeds. Even then they show far lower levels than those of ragweed in most places in the central states, and far less than one would judge from observation of the thousands of square miles of sagebrush in the West. Sun Valley itself lies among the foothills covered with a pure stand of mountain sagebrush. Thus, sagebrush production proves to be far less per acre than ragweed—probably no more than one-tenth as much. The record for Nashville, Tenn., is unique. Here annual sage (*Artemisia annua*), a green, sweet-scented, fern-like weed, with little resemblance to its sagebrush relatives of the West, is unusually abundant. Its clinical evaluation is difficult because its season of pollination coincides with that of ragweed, and skin reactions to annual sage pollen, unaccompanied by ragweed reactions, are extremely rare. The season of anthesis of the sages differ with the species and locality, but most of them pollinate in the fall.

GOOSEFOOTS AND AMARANTHS

The principal hay fever offenders in the goosefoot (chenopod) family are the tumbleweeds: Russian thistle (*Salsola pestifer*) and firebrush, or fireweed (*Kochia scoparia*), of the dry-farming areas of the Great Basin, sometimes referred to as the Dust Bowl. Russian thistle is also abundant locally throughout the Rocky Mountain region, while firebrush is slowly extending its range eastward, particularly in the larger cities. The outstanding members of the amaranth family, as far as air pollution is concerned, are Palmer's amaranth (*Amaranthus palmeri*) of the Southwest and western water hemp (*Acnida tamariscina*) of the corn states.

Since the pollens of both goosefoots and amaranths are so similar in microscopic appearance and their antigenic qualities so nearly identical, they are frequently counted and reported (Fig. 3) as a group rather than by separate species. In the Southwest heavy local exposure to the pollen of Palmer's amaranth, or careless weed, is frequent in cultivated fields in the late fall, while Russian thistle is a very minor offender.

At Goodland, Kan., as in most places in the Great Basin area, the goosefoot-amaranth season begins definitely in early July and lasts well into September. Here Russian thistle pollen has proved far more active clinically than that of any other local species, even more than that of the local prairie ragweed, otherwise known as burweed marsh elder (*Iva xanthifolia*). It is most interesting that in this area, in spite of ragweed pollen concentration as high as is frequently encountered in Boston (Fig. 2), less than one case out of 25 of local hay fever is complicated by sensitiveness to ragweed. A possible explanation of this situation may be that prairie ragweed is not a ready sensitizer like the other ragweeds. The assumption is hardly tenable, however, since most ragweed-sensitive persons in areas where prairie ragweed does not exist will show marked skin reactions to its pollen—frequently as strong as to that of short and giant ragweeds. At any rate, there is plenty of evidence that Russian thistle pollen is a more active sensitizer than that of any species of ragweed.

Western water hemp pollen is as abundant as ragweed pollen at Wichita, Kan. (Fig. 3). It appears in appreciable percentages at Lincoln and Omaha and sometimes at St. Louis. Although western water hemp is a member of the amaranth family, its pollen is not nearly as allergenic as that of Palmer's amaranth. Pigweeds and lamb's quarters are common weeds of fields, gardens, and waste places throughout North America. While their pollens interreact with those of the other goosefoots and amaranths already discussed, their output is evidently too small for clinical consideration. Clinical symptoms traceable to these pollens are extremely rare or absent in the eastern half of the United States. Obviously, it is not difficult to find refuge from the goosefoots and amaranths.

Hemp (*Cannabis sativa*), popularly known as marijuana, is so common in the western half of Iowa and extreme eastern Nebraska, and its pollen is so abundant and allergenic, that it constitutes an outstanding example of an active pollen of strictly local distribution (distribution not shown on maps).

7. Florida State Board of Health: About Breezes and Sneezes, Florida Health Notes, Vol. 43, No. 2, February, 1951.

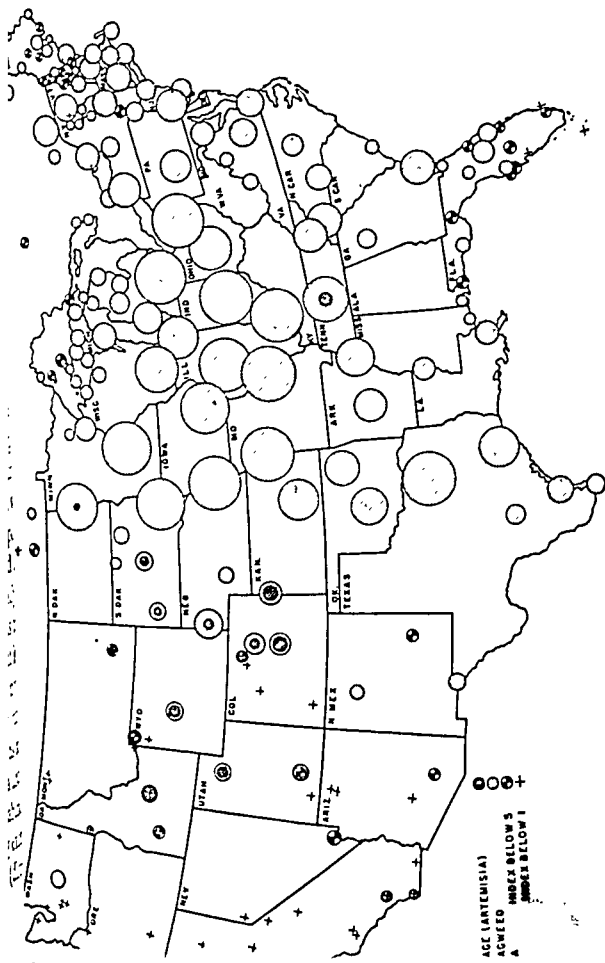


Fig. 3.—Typical ragweed and sage (Artemisia) pollen records. Area of discs denotes comparative total annual fall in each locality.

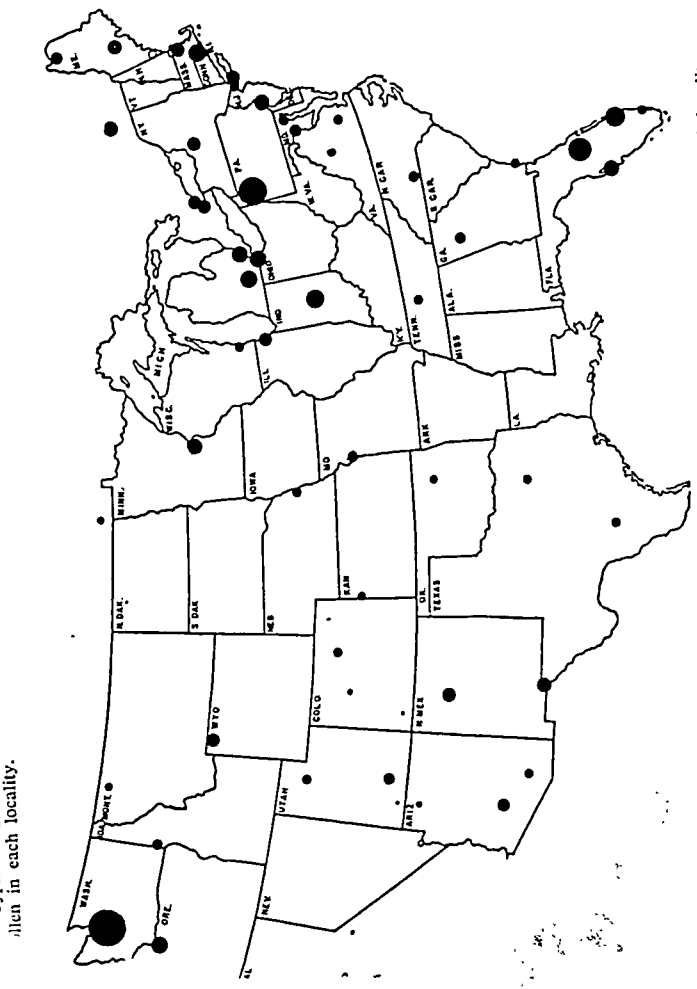


Fig. 4.—Typical tree pollen records. Area of discs denotes comparative total annual fall in each locality.

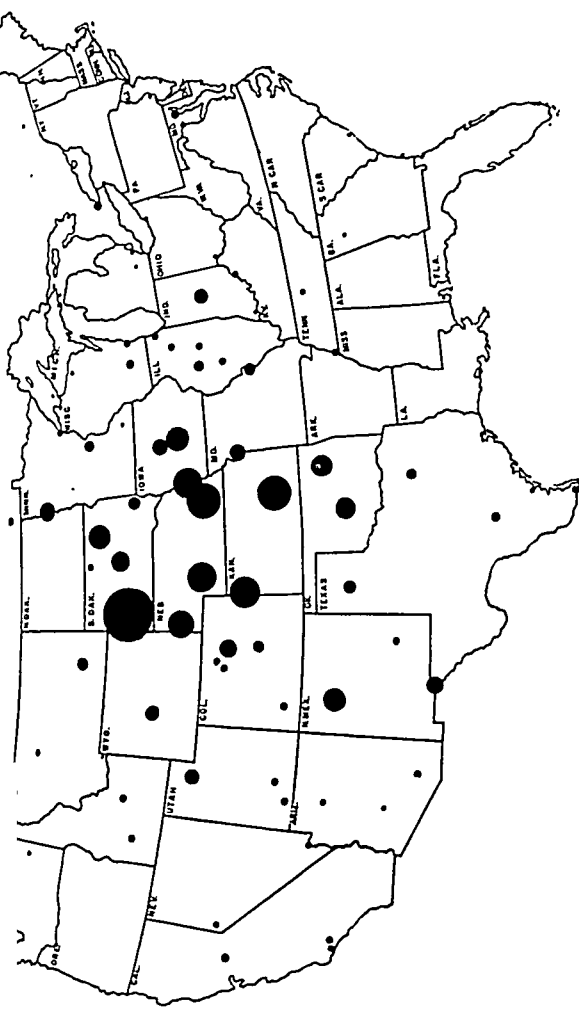


Fig. 5.—Typical records for all species of goosefoot (Chenopodiaceae) and amaranth (Amaranthaceae) pollen. Area of discs denotes comparative total annual fall of pollen in each locality.

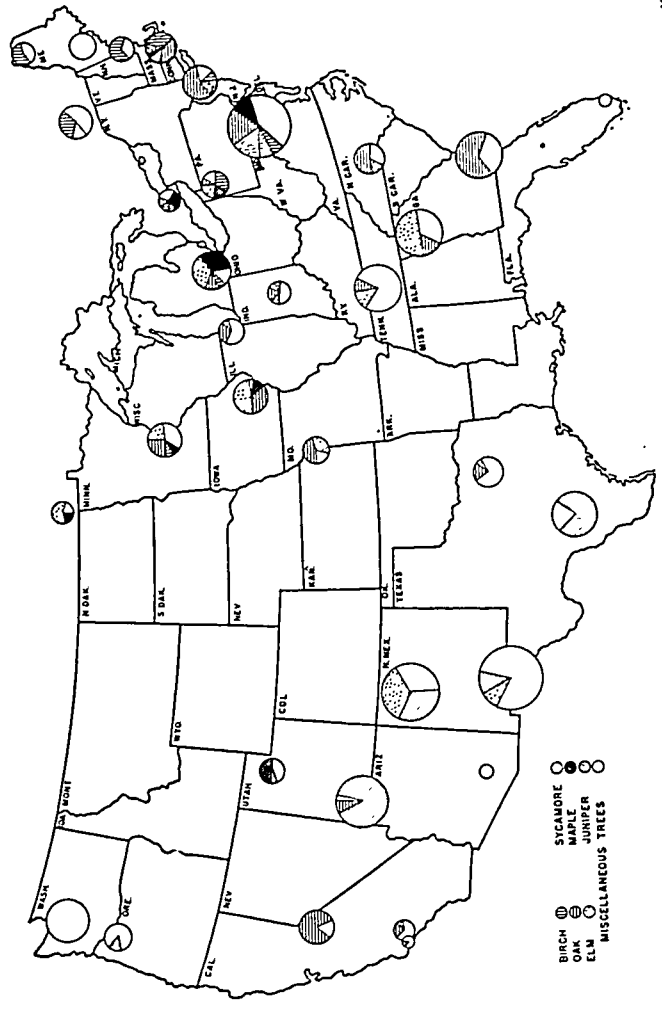


Fig. 6.—Typical tree pollen records. Area of discs denotes comparative total annual fall of all types of tree pollen. Proportions of six more important types are shown by comparative area of segments.

GRASS POLLEN

The grass pollen map (Fig. 4) is an experiment—a risk as far as interpretation is concerned, not because the local records are less numerous but because the totals are surprisingly small as compared with the annual totals for ragweed. Perhaps this is explained by the fact that wild grasses shed very little pollen and by the comparatively small acreage of freely pollinating cultivated grasses. It is true that grass pollen grains are relatively heavy and are not as readily dispersed in the air as are the lighter pollens like ragweed. Oddly enough, it has been found that in the northern and northeastern states, where the grass pollen content of the air averages only about 10% of that of ragweed, the ratio of clinical cases of grass sensitiveness to ragweed cases is actually about 1 to 10.

Unfortunately, there is little opportunity for complete escape from grass pollen except by staying indoors with windows and doors closed or taking a sea voyage. Grasses grow luxuriantly even in high mountain valleys and are a menace in irrigated desert areas. The heavy rainfall in the Pacific Northwest is particularly conducive to the growth of the meadow grasses, as evidenced by the Seattle grass total (Fig. 4), which exceeds that of any community thus far reported. In the Pacific Northwest, the north central states, and the Atlantic seaboard from Massachusetts to Virginia, the active season runs from about the middle of May until the middle of July.

Year around pollination of Bermuda grass is encountered in the extreme Southwest. While Bermuda grass pollen is probably the most active clinically of any grass pollen, and one of the most troublesome pollens of Arizona and southern California, it is produced in relatively small amounts and ripens very close to the ground. While air tests often reveal an average of less than 2 grains of Bermuda grass pollen per cubic yard of air through the ear, close contact with the grass on lawns and irrigated fields can cause severe symptoms in sensitized persons. Thus, wide differences in the time and length of season and in the relative prevalence of grass pollen (all species) in widely separated areas are emphasized by the atmospheric studies.

TREE POLLENS

The tree pollens as a group are mostly an allergic headache to the physician. As a group, three pollens are much less toxic than those of the weeds and grasses already discussed. The pollens of all pines, firs, and spruces, of hemlock, mountain hemlock, and deodar cedar are so inactive that pollen researchers seldom take the trouble to record them, and most allergists omit them entirely from their test kits. Of the conifers, it seems that only the juniper pollens and those morphologically similar types, such as incense cedar (*Libocedrus decurrens*), are active. Even those broad-leaved trees which produce pollen in large amounts account for only very occasional severe sensitization. Moreover, in many localities the list of potential offenders is large—not only a long list of oak species but numerous unrelated genera, such as elms, maples, sycamore, ash, hickory—thus complicating skin testing for true hay fever occurring in late winter and early spring. Another difficulty is that the seasons of tree pollination are not very dependable. A given species may vary greatly in time and intensity of production from year to year with the changeable weather of early

spring. Therefore, the tree pollen records shown in tabular form and in graphic form on the map (Fig. 5) are not to be regarded as necessarily typical.

The maximum variety and quantity of tree pollens in any reported annual study were found in the Washington, D. C., tabulation (Table 1). Here the annual catch of nearly 20 distinct tree pollens doubles the production of ragweed, and the season lasts twice as long. Yet comparatively few Washington residents suffer severely with pollen allergy while the trees are in bloom. The oaks around the capitol led all trees in production in 1950, while in 1949 paper mulberry pollen was more abundant than that of any other plant, including the ragweeds.

Elms furnish a good example of the great variation in time of anthesis in various places due to latitude and climate, as well as to differences of habit of native and imported species. In the Gulf states, American elm begins to bloom in early January; at Washington, D. C., in February; at Montreal and Portland, Ore., in April. Texas scrub elm (*Ulmus crassifolia*) and certain species of Chinese elm used in the Southwest shed their pollen in late summer and fall.

Junipers and related conifers are interesting sources of large amounts of very active allergenic pollen, beginning in December and continuing to early spring. Vast stretches of juniper woods are found in the thinly populated areas of the Southwest, but mountain cedar (*Juniperus sabinoides*) pollen is a menace throughout central Texas. Incense cedar, which flourishes in the Sierras, is a frequent sensitizer of winter residents and winter visitors at Yosemite National Park (see graphic data for San Antonio and El Paso, Texas; Albuquerque, N. Mex.; and Zion National Park in Fig. 5).

Much remains to be done in filling in the gaps in the tree pollen picture, particularly in the almost treeless Great Basin. More data are needed from all areas. Wax myrtle (*Myrica cerifera*), a native shrub of the middle and south Atlantic seaboard, sheds pollen abundantly, but because of the scarcity of pollen records during early spring along the Atlantic coast this pollen has been counted only at St. Simons Island, Ga. Its allergenic qualities have not been studied nor have those of bald cypress (*Taxodium distichum*).

Since it has been impossible within the limits of this paper to present more than a glimpse of the results of the extensive work of pollen researchers during a quarter of a century, requests for detailed summaries and for complete data, as available for any particular locality, will be answered as promptly as possible if directed to the Pollen Survey Committee of the American Academy of Allergy, Abbott Laboratories, North Chicago, Ill.

The Founder of Experimental Physiology.—Galen was one of the most brilliant intellects applied to medicine, and he was the founder of experimental physiology and the greatest Greek physician after Hippocrates. His observations on the physiology of the central nervous system are probably the best example of his keen sense of observation. He was a versatile, many-sided man of talent and a skilled practitioner of his time, although he left no good account of his clinical cases. He had a roving disposition, as had many of the famous physicians of that period. After his death European medicine remained at a dead level for nearly fourteen centuries.—Donald C. Balfour, *The Lister Epoch in Medicine*, *Canadian Medical Association Journal*, November, 1951.

FUNCTIONAL OBSTRUCTION OF EFFERENT LOOP OF JEJUNUM FOLLOWING PARTIAL GASTRECTOMY

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Subtotal or partial gastric resection is the routine for the majority of operable carcinomas of the stomach and, in the hands of some surgeons, is the operation of choice for intractable gastric or duodenal ulcer.¹ The operative mortality has steadily declined during the past two decades. Glenn and Harrison² reported one death in 100 consecutive cases of gastric resection for peptic ulcer in 1948. St. John and co-workers¹ noted a mortality of 4.6% in 394 cases of partial gastric resection for ulcer during the 10 years ending in 1945.

Along with operative mortality, the incidence of postoperative complications has diminished. This undoubtedly has resulted from better preparation of the patient for operation and better understanding of the pathological physiology resulting from the operative procedure.

One puzzling postoperative complication is an apparently functional obstruction of the efferent loop of jejunum. Repeated postoperative vomiting has been encountered in occasional patients for many years, but the association of this symptom with spasm of the efferent loop, demonstrable by x-ray examination, was not recognized in our radiological and surgical services until 1944.

In the majority of these cases convalescence is satisfactory for 8 to 12 days. Then, for no obvious reason, the patient begins to complain of epigastric fullness, particularly after eating, and nausea and vomiting. In a minority these symptoms may appear earlier or later. The symptoms are relieved by gastric evacuation by a tube but recur after a few hours. Continuous suction evacuation of the stomach by a nasogastric tube gives persistent relief but prevents the patient from getting nourishment. The use of intravenous solutions suffices to maintain the protein and electrolytes at satisfactory levels until the symptoms disappear. This usually occurs between 2 and 10 days after onset, but it may take longer.

X-RAY EXAMINATION AFTER PARTIAL GASTRECTOMY

In this discussion the remaining proximal portion of the stomach will be referred to as the stomach pouch, the portion of jejunum into which the stoma opens will be called the stoma loop. The efferent loop of jejunum passes caudad away from the stomach pouch, and the afferent loop leads to the stomach pouch from loops proximal to the anastomosis.

The stomach pouch cannot produce peristaltic waves such as are seen normally in the lower half of the stomach. It must empty largely by gravity into the stoma loop and into the efferent loop of jejunum.

When distended with food, the stomach pouch expands much more on the greater curvature than on the lesser curvature side. The anastomosis on the greater curvature side lies lower than the lesser curvature; therefore, drainage of the stomach pouch is easier when

the efferent loop of jejunum is connected to the greater curvature side of the anastomosis.

The radiological examination after partial gastrectomy should be done in the morning after the patient has fasted overnight, with the patient erect behind the fluoroscopic screen. When conditions are normal, no residual fluid is found in the stomach pouch, and the first swallow of barium passes immediately or after a momentary delay into the efferent loop of jejunum. The caliber of this efferent loop is the same as that of more



Fig. 1.—A normally functioning anastomosis of the Polya type with the efferent loop extending from the lesser curvature side of the stomach pouch. The efferent loop is the same average width as the more distal loops of jejunum.

distal loops of jejunum (fig. 1). As additional barium is given, a contraction may appear in the efferent loop that temporarily holds back the flow of opaque fluid. Usually, however, the stomach pouch will be practically empty after a few minutes in the erect position. In the horizontal position the emptying of the stomach pouch is slower. These remarks apply when the efferent loop leads away from the greater curvature side of the stomach pouch, as in the Hoffmeister type of anastomosis.

Read before the Section on Radiology at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 13, 1951.

From the Department of Radiology, College of Physicians and Surgeons, Columbia University, and the Radiological Service of the Presbyterian Hospital.

1. St. John, F. B.; Harvey, H. D.; Ferrer, J. M., and Sengstaken, R. W.: Results Following Subtotal Gastrectomy for Duodenal and Gastric Ulcer, *Ann. Surg.* 128: 3-14 (July) 1948.

2. Glenn, F., and Harrison, C. S.: The Surgical Treatment of Peptic Ulcer, *Ann. Surg.* 132: 36-48 (July) 1950.

If the Polya type of anastomosis has been done with the efferent loop leading from the lesser curvature side, the emptying of the stomach pouch is much slower. The first swallow of barium fills the stoma loop, which passes obliquely from the greater curvature side of the stoma upward and toward the right. The opaque mate-

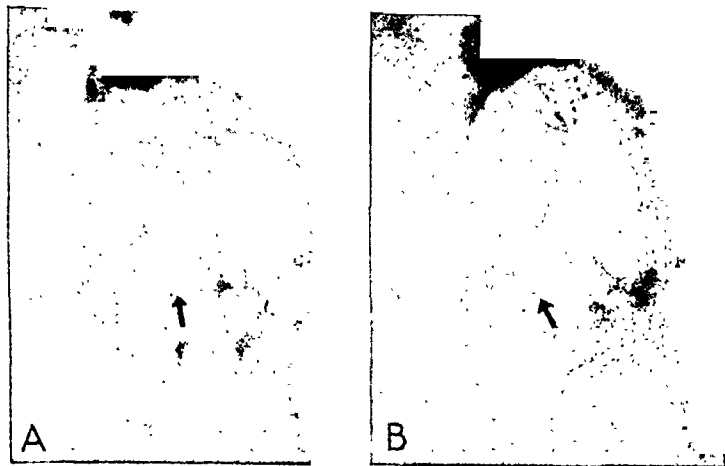


Fig. 2 (case 1).—*A*, spasm of the efferent loop (arrow). *B*, the same patient approximately 10 weeks after partial gastrectomy with the efferent loop (arrow) normal in width.

A man, 51, had a partial gastrectomy for duodenal ulcer. An antecolic Polya type anastomosis was done, with the efferent loop extending medially from the lesser curvature. Convalescence was satisfactory until the ninth postoperative day, when the patient began to vomit. X-ray examination on the 12th postoperative day disclosed an obstruction at the beginning of the efferent loop. After considerable delay a little barium passed through the very narrow efferent loop to the more distal loops of jejunum, which were normal in width. A 24 hour residue of barium was found in the stomach pouch. No vomiting occurred after the 14th postoperative day.

rial usually first passes a short distance downward and to the left into the afferent loop and is usually moved back upward toward the anastomosis by peristaltic contractions. Peristaltic movements in the stoma loop are required to expel the opaque material to the right and ward into the efferent loop. These movements are so effective in the stoma loop as they are in the intact estine, because the former opens through the anastomosis into the stomach pouch. With this arrangement,

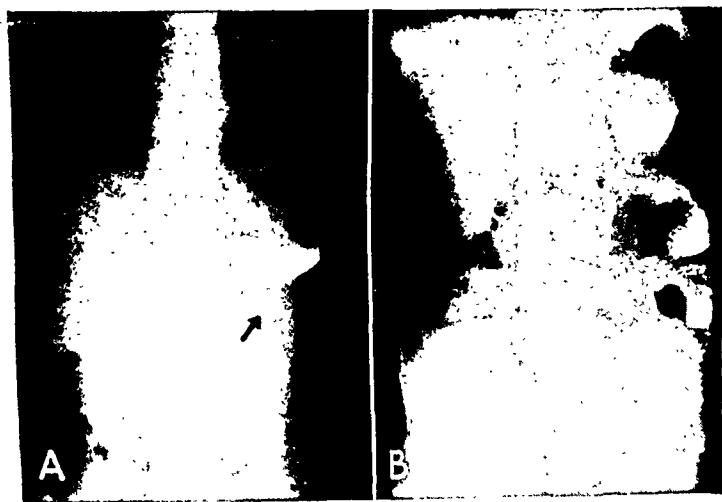


Fig. 3 (case 2).—*A*, spasm of the efferent loop (arrow). *B*, the same patient on the 39th postoperative day and 21 days after vomiting ceased. The efferent loop (arrow) has relaxed and is passing barium but is still only about half the width of the lower loops of jejunum. A nonopaque fluid level lies above the barium, a residue of overnight fasting fluid.

A man, 52, had a partial gastrectomy for a bleeding duodenal ulcer. A retrocolic Hoffmeister type anastomosis, with the efferent loop extending downward and to the patient's left, was done. Vomiting began on the seventh postoperative day. The roentgenogram in *A* was taken with the patient erect on the 14th postoperative day. Above the barium is a large amount of nonopaque retained fluid, at the top of which is a small amount of gas. Four days later, on the 18th postoperative day, vomiting ceased

i. e., with the efferent loop extending to the right from the lesser curvature side, the stomach pouch empties more freely when the patient lies on the right side.

POSTOPERATIVE SPASM OF EFFERENT LOOP

When symptoms consistent with unsatisfactory function of the anastomosis develop after partial gastrectomy, it is important to differentiate the syndrome under discussion from mechanical or paralytic ileus, in which distention of the small intestine distal to the efferent loop occurs. X-ray examination should be done, and the radiologist should be informed as to the type of anastomosis the patient has.

In this syndrome the stomach pouch usually contains a large amount of nonopaque fluid after the patient has fasted overnight. This fluid consists of gastric secretions and bile and pancreatic juice, which enter freely by the afferent loop but cannot be expelled caudad. The first swallow of barium passes along the lesser curvature into the stoma loop. It is held up not at the anastomosis itself but at the junction of the stoma loop and the efferent loop or in the efferent loop 2 to 3 in. (5 to 7.5 cm.) beyond the anastomosis. In some cases a

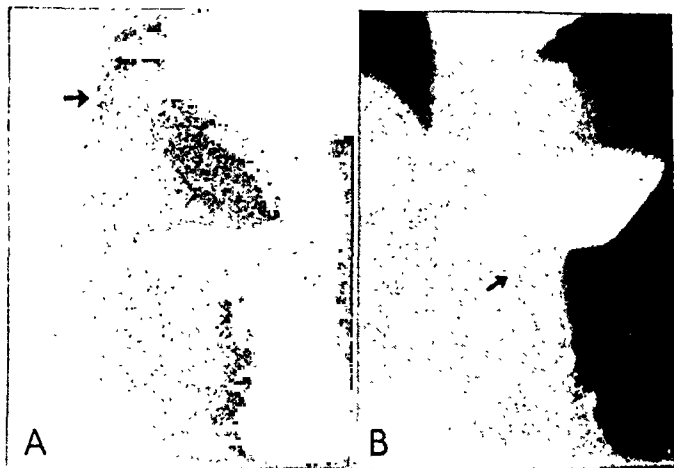


Fig. 4.—*A*, temporary obstruction of the efferent loop with an accumulation of overnight fasting fluid (arrow) above the barium, but without symptoms, in a man, 55, who had a retrocolic Hoffmeister anastomosis following partial gastrectomy for carcinoma of the stomach. This examination was done on the eighth postoperative day. *B*, narrowing of the efferent loop of jejunum (arrow) extending downward and to the left from the anastomosis. The spasm of the efferent loop partially relaxed after the third swallow of barium, two or three minutes after the roentgenogram shown in *A* was taken.

little opaque material will pass through the efferent loop into more distal portions of the jejunum in a few minutes to several hours. In other cases the barium suspension is held in the stomach pouch indefinitely until it is vomited or is removed by suction through a tube. If a little barium passes through, the lumen of the efferent loop appears very narrow, one-fourth or less of the normal caliber (fig. 2*A* and 3*A*). This narrowing extends for several centimeters, beyond which the lumen becomes normal in width. The mucosal pattern in the narrowed zone may be either normal or somewhat irregular. Examination after the patient has fully recovered discloses prompt emptying, with the efferent loop normal in width (fig. 2*B* and 3*B*).

Four symptomless patients were examined in the erect position 7 to 10 days after partial gastrectomy. Three of them had considerable residual fluid in the stomach pouch after fasting overnight (fig. 4*A*), and one had no

fluid. All had moderate narrowing of the efferent loop of jejunum extending up to 6 or 7 cm. below the anastomosis (fig. 4B). This indicates that temporary, probably intermittent, delay in emptying the stomach pouch may occur without producing symptoms.

COMMENT

Glenn and Harrison encountered 14 instances of "postoperative gastric retention" in 100 cases of gastric resection for ulcer during 1948. They describe the retention—presumably meaning the symptoms—as occurring from 1 to 14 days following operation in 11 of the 14 cases; in the other three cases the longest time was 30 days. Of the 100 cases discussed by these writers, the Polya type operation was used in 73, the Hoffmeister type in 20, and other methods in the remaining 7. All the 14 patients had the Polya type operation, either anterior or posterior.

St. John and co-workers reported a study of 394 cases of partial gastric resection for ulcer performed between 1936 and 1945 inclusive. They refer to 47 of these patients who had some postoperative symptom attributable to obstruction of the efferent loop, but they give no detailed information as to time of onset or duration. Most of their patients had the anterior Polya type operation. Toward the end of the decade the Hoffmeister type operation was used in the majority of cases. They have the impression that postoperative complications were less frequent after the retrocolic Hoffmeister operation than they were after the anterior Polya operation.

St. John and co-workers mention spasm of the afferent loop in two cases. I have not personally encountered a case in which spasm of the afferent loop was demonstrated by x-ray methods in association with these symptoms. In fact, when the syndrome under discussion was present, barium entered the afferent loop easily in the patients I have seen.

In the past a second operation was often done for persistent vomiting. Sometimes adhesions were found involving the efferent loop, and other times no visible abnormality was discovered to which the obstruction could be attributed. Freeing of the adhesions was assumed to be the reason for the disappearance of the symptoms some days after the second operation. However, in two cases I have personally investigated, the site of obstruction, shown by the barium examination, was proximal to the site of the adhesion. In one instance, after removal of the adherent omentum, a tube was pulled through the stomach pouch into the efferent loop at the second operation, for the purpose of injecting nutriment into the lower jejunum, but the narrowing of the efferent loop and the obstruction to swallowed barium persisted for at least four days. In cases in which nothing is found at the second operation, the symptoms disappear in about the same length of time. Of interest is the fact that the narrowing of the lumen, so obvious at the barium examination, is not seen by the surgeon at the time of the second operation. Furthermore, the time interval between the partial gastrectomy and the onset of symptoms is the same in cases with, as in those without, adhesions involving the efferent loop.

Inasmuch as the obstruction of the efferent loop is relieved spontaneously after a period of days, the diffi-

culty is apparently produced by spasm or failure of the efferent loop to relax. It seems logical to assume that this obstruction is the result of a localized physiological disturbance in the intestinal wall resulting from the operation. For this a hypothetical explanation can be offered, based on two facts: 1. Part of the intramural nervous system consists of nerve fibers that are not connected with either the sympathetic or the parasympathetic system. These fibers connect physiologically one segment of intestine with another over a distance of several centimeters, and the normal direction of flow of any stimulus is caudad. 2. A mechanical stimulus of the wall of the intestine, as by pinching, causes a contraction. Does the mechanical stimulus of the incision and the sutures in the wall cause a contraction in the efferent loop? A similar phenomenon is seen in association with peritoneal adhesions involving the small intestine.³ However, the time lag of several days between the operation and the onset of symptoms remains to be explained. Why, in the great majority of cases, does it take that length of time for the stimulus to produce sufficient spasm to cause symptoms of obstruction? Why does this phenomenon appear only in a small percentage of patients after partial gastrectomy, although the same or a similar mechanical stimulus is present in all? For these questions satisfactory answers do not seem to be immediately available. Possibly an accessory factor is present that makes the mechanical stimulus, present in all the cases, more effective in some. Barden, Raydin, and Frazier⁴ emphasized the importance of edema of the jejunal wall resulting from hypoproteinemia as a factor in retardation of emptying after gastroenterostomy. However, in more recent years care has been taken to maintain the blood protein well above the edema level during the postoperative period, and it seems unlikely that this is a factor in the spasm of the efferent loop. It is known that a loss of potassium follows any operation⁵; this is associated with edema and a disturbance in motor function of the small intestine, characterized by evidence of a mild paralytic ileus. No evidence is available that either of these conditions plays a part in the syndrome under discussion.

Whatever the mechanism may be, the obstructive spasm of the efferent loop appears to be a self-limited physiological disorder, provided the blood protein and electrolytes are maintained at normal levels by appropriate methods and the distention of the stomach pouch is relieved by suction evacuation.

SUMMARY

A functional obstruction of the efferent loop of jejunum resulting from spasm occurs in a small percentage of cases after partial gastrectomy. The symptoms, epigastric fulness, nausea, and vomiting, begin in the great majority of cases during the second postoperative week.⁶

3. Golden, R.: Some Problems in Abnormal Intestinal Physiology Associated with Peritoneal Adhesions and Ileus Pancoast Lecture, *Am. J. Roentgenol.* 56: 555-568 (Nov.) 1946.

4. Barden, R. P.; Raydin, I. S., and Frazier, W. D.: Hypoproteinemia as a Factor in the Retardation of Gastric Emptying After Operations of Billroth I or II Types, *Am. J. Roentgenol.* 38: 196-202 (July) 1937.

5. Randall, H. T.; Habib, D. V.; Lockwood, T. " and V. " Potassium Deficiency in Surgical Patients, 1949.

6. At the Presbyterian Hospital it "the nine day disorder."

They disappear spontaneously in a few days, in the majority, to two to three weeks, in the minority of cases. X-ray examination discloses spasm of the efferent loop of jejunum when the symptoms are present, with delay in emptying the stomach pouch. After the symptoms disappear, the caliber of the efferent loop is essentially normal. The spasm of the efferent loop is apparently due

to a localized temporary disturbance in muscle function resulting from the necessary surgical trauma to the jejunum in making the anastomosis. This syndrome appears to develop less frequently after procedures requiring a shorter incision than in those requiring a longer one in the jejunal wall.

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PULMONARY CHANGES IN UREMIA

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and

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Alterations occurring in the lung associated with uremia have received attention only in recent years. A search of the literature reveals references to 34 cases. Ehrich and McIntosh, in 1932, studied the lung changes in three patients who died of Bright's disease.¹ Subsequent reports described the chest roentgenograms of the lung in patients with uremia.² The features of this condition were characteristically those of increased densities, confined predominantly to the hilar areas of the lungs in a bilateral symmetrical fashion, with clear basal and peripheral zones. This picture was described principally by roentgenologists, who considered the condition a form of pulmonary or "uremic" edema. The picture was sometimes seen in hypertensive patients in whom heart failure developed during the course of uremia. Pulmonary densities were often associated with early death. Recovery occasionally followed alleviation of both heart failure and the azotemic state. There have been few histopathological studies of the uremic lung.¹ Epstein and Greenspan³ described hyaline membranes in the lungs of a patient with glomerulonephritis. They called attention to the marked resemblance of the lung to similar changes occurring in rheumatic pneumonia. More recently, Doniach⁴ reported on a group of patients with "uremic" edema of the lungs and described the alveolitis in the lung.

Two of us (H. B. and E. S.) recently reported on a group of patients with uremia who had pulmonary changes.⁵ These patients showed abnormal shadows on chest roentgenograms during the course of azotemia,

which was due to various causes. Further studies have since been conducted in an attempt to clarify the pathogenesis and clinical features of the uremic lung. In the three year period 1948 to 1950, a group of eight patients with pulmonary changes associated with uremia were observed at the Jewish Memorial Hospital. We believe that these changes occur more frequently than is generally recognized.

ROENTGEN PICTURE

The roentgen features seen in our patients followed, in general, the pattern described by other authors. The pulmonary densities were generally extensive and confined to the inner lung zones (fig. 1). Although most of the cases showed a "butterfly" distribution, occasional



Fig. 1.—Roentgenograms of patient with acute glomerulonephritis associated with bilateral pulmonary densities. Picture on the right shows increase in pulmonary densities shortly before death.

basal involvement was also noted. The densities were transient in some patients and were associated with left ventricular failure. Alleviation of heart failure, in some cases, resulted in the disappearance of the densities.

CLINICAL PICTURE

All the patients observed in this series died. The appearance of the pulmonary densities during uremia seems to indicate an ominous complication. An enlarged cardiac shadow was usually present. The appearance of the pulmonary shadows was occasionally a surprise to the clinician. Although the roentgen picture simulated pulmonary edema, as described by roentgenologists, the patients showed none of the characteristics of this disease. Some patients had mild dyspnea, and physical findings in the chest were minimal. In other patients, the

From the Medical Services of the Jewish Memorial Hospital, New York.

Read before the Section on Diseases of the Chest at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 13, 1951.

This work has been aided by a grant from the David Schwartz Research Fund. Two of the cases in this report were studied through the assistance of Drs. DeAngelis, Alesio, Harris and Rudnikoff of Yonkers, N. Y.

1. Ehrich, W., and McIntosh, J. F.: The Pathogenesis of Bronchiolitis Obliterans: Observations in Cases of Bright's Disease, *Arch. Path.* **13**: 69 (Jan.) 1932.

2. Roubier, C., and Plauchu, M.: Sur certains aspects radiographiques de l'edème pulmonaire chez les cardio-rénaux azotémiques, *Arch. méd.-chir. de l'app. respir.* **9**: 189, 1934. Rendich, R. A.; Levy, A. H., and Cove, A. M.: Pulmonary Manifestations of Azotemia, *Am. J. Roentgenol.* **40**: 802, 1941.

3. Epstein, E. Z., and Greenspan, E. B.: Rheumatic Pneumonia, *Arch. Int. Med.* **68**: 1074 (Dec.) 1941.

4. Doniach, I.: Uremic Edema of the Lungs, *Am. J. Roentgenol.* **58**: 620, 1947.

5. Bass, H. E., and Singer, E.: Pulmonary Changes in Uremia, *J. A. M. A.* **144**: 819 (Nov. 4) 1950.

roentgen findings were most pronounced, and dyspnea was severe. These patients showed evident oxygen want, and death was apparently due to anoxia.

PATHOLOGICAL FEATURES

Grossly, the uremic lungs showed a consolidation of the inner aspect that stopped abruptly below the periphery of the lung. The outer lung zones were normally aerated. On section, no evidence of infection or arteritis was found. Hyaline membranes and hyaline deposits in the alveoli were common features (fig. 2 and 3). The findings were more evident in patients with glomerulonephritis. In the more advanced cases, particularly if the disease had been severe and the patient had lived long, hyalinization of the intra-alveolar exudate was extensive. The alveolar spaces were filled by plugs of rounded hyaline bodies (fig. 2). These findings explain the profound and unalleviated dyspnea from which these patients suffered and suggest that the cause of death in some patients was anoxic rather than renal.

These findings were also described in patients with influenza in the pandemic of 1918, in streptococcal pneumonias, as a result of inhalation of noxious and poisonous gases, in early radiation pneumonitis, in "vernix" or so-called aspiration pneumonia of the newborn, and

perimortal work by Farber indicates that the hyaline membrane may be the result of the mechanical dispersion of this foreign material toward the periphery of the alveolus by air violently inspired. These hyaline deposits have attracted the attention of pediatricians, who have considered intrauterine anoxia as a factor in the patho-



Fig. 2.—Photomicrographs of mononuclear alveolar exudate and hyaline deposits seen on section (from same patient as in figure 1).

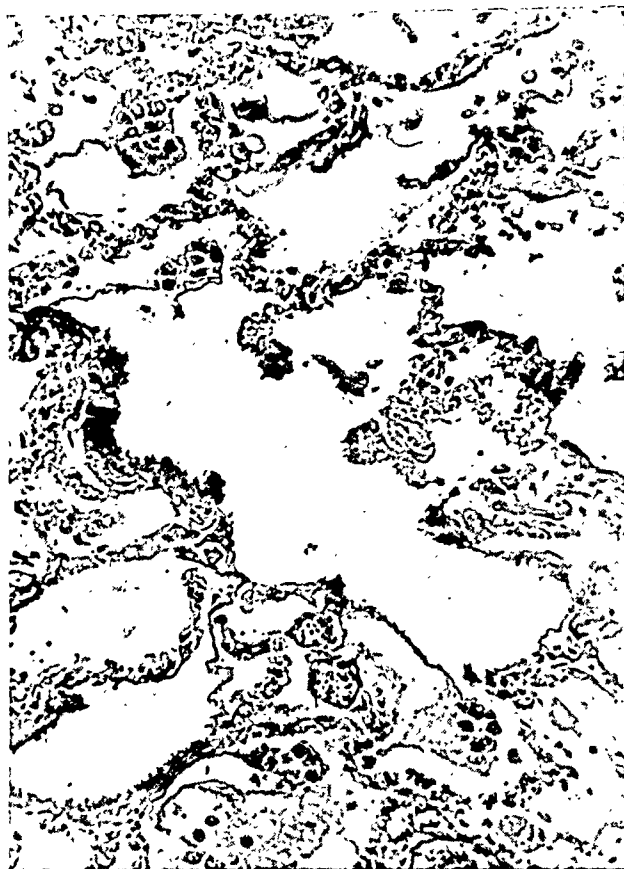


Fig. 3.—Photomicrograph of hyaline membranes seen near periphery of lung (from same patient as in figure 1).

genesis of aspiration pneumonia of the newborn.⁷ More recently, similar findings were described in a peculiar pneumonia associated with retinal cytooid bodies.⁸

The hyaline membranes and hyaline deposits in the uremic lung are similar to those found in the conditions described above. The resemblance to the rheumatic lung is striking. In addition, the roentgen features of the uremic lung and rheumatic pneumonia are similar.⁹

COMMENT

The similarity of these findings in such a variety of conditions suggests a common pathogenesis. The factor of capillary damage and altered capillary permeability has been suggested by others.¹⁰ It is reasonable to assume

6. Farber, S., and Wilson, J. L.: The Hyaline Membrane in the Lungs: A Descriptive Study, *Arch. Path.* 1-1: 437-449 (Oct.) 1932.

7. Miller, H. C., and Hamilton, R. T.: Pathogenesis of the "Vernix Membrane": Its Relation to Aspiration Pneumonia in Stillborn and Newborn Infants, *Pediatrics* 3: 735, 1949. Miller, H. C., and Jennison, M. H.: Study of Pulmonary Hyaline-Like Material in 4,117 Consecutive Births: Incidence, Pathogenesis, and Diagnosis, *Pediatrics* 5: 7, 1950.

8. Tumulty, P. A.; Berthrong, M., and Harvey, A. M.: A Peculiar Pneumonia Associated with Retinal Cytooid Bodies, *Bull. Johns Hopkins Hosp.* 88: 239, 1951.

9. Seldin, D. W.; Kaplan, H. S., and Bunting, H.: Rheumatic Pneumonia, *Ann. Int. Med.* 26: 496, 1947.

10. Barden, R. P., and Cooper, D. A.: The Roentgen Appearance of the Chest in Diseases Affecting the Peripheral Vascular System of the Lungs: Conditions Associated with Increased Vascular Permeability, *Radiology* 51: 44, 1948. Epstein and Greenspan.³

in rheumatic pneumonia. Farber⁶ has described hyaline membranes and masses of amorphous eosin-staining hyaline material in the air spaces. These masses of amorphous material were similar in appearance and staining reactions to the material in the hyaline membranes. Ex-

that factors of infection, anoxia, hyperergy, chemical irritation, and radiation injury all produce similar damage to the pulmonary capillary bed and thus account for the similar pathological findings. It has been pointed out² that the lung changes in uremia occur in only a small percentage of patients with azotemia; the reason for this is not apparent. In the patients we observed, the most striking changes in the lungs occurred in cases associated with acute episodes of glomerulonephritis. The work of Ehrich and McIntosh suggests that repeated insults to the pulmonary capillary bed may occur in chronic glomerulonephritis, culminating in bronchiolitis fibrosa obliterans.

The pulmonary changes herein described as associated with the azotemic states are brought about by altered capillary permeability and are more apt to occur in glomerulonephritic uremia. The importance of these alterations lies in their resemblance to other pulmonary diseases. The most frequent symptoms are dyspnea, which may be severe, and, occasionally, bloody sputum. Fever is not a predominant finding. The pulmonary densities resemble those of tuberculosis, sarcoidosis, pneumoconiosis, fungous diseases, and the various pneumonias.

In one case, hemoptysis was an outstanding symptom and led to an initial diagnosis of pulmonary neoplasm. In another case, the extensive pulmonary densities were the basis for a diagnosis of virus pneumonia, and treatment with various antibiotic drugs was unsuccessful. The finding of these densities in a patient with uremia should lead one to expect a fatal outcome. Positive pressure oxygen, relief of heart failure, and treatment of the azotemic state and acidosis may bring about a recession of the condition. Treatment with antibiotics is usually of no value.

SUMMARY AND CONCLUSIONS

A group of eight cases of "uremic lungs" was observed, and an attempt was made to correlate the clinical, roentgenological, and pathological findings.

The lung changes in uremia follow a rather consistent pattern from the clinical, roentgenologic and pathological viewpoints. These changes are not specific and are also found in other conditions brought about by altered pulmonary capillary permeability. We believe that these pulmonary alterations occur more frequently than is generally known. The recognition of the "uremic lung" is important from the standpoint of prognosis and its resemblance to other pulmonary diseases.

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TRAUMATIC ARTERIOVENOUS ANEURYSM ASSOCIATED WITH STREPTOCOCCIC SEPTICEMIA

REPORT OF A CASE WITH CURE FOLLOWING PENICILLIN THERAPY AND OPERATION

Mark H. Williams, M.D., Binghamton, N. Y.

Endocarditis or endarteritis occurs rather commonly in patients having congenital cardiac defects. Those having a patent ductus arteriosus or interventricular septal defect are especially susceptible to these complications.¹ Examples of endarteritis and septicemia produced by other arteriovenous fistulas are rare. The first patient in the latter category to be cured after operation was reported by Rienhoff and Hamman² in 1935. A second patient cured by operation was reported by Touroff³ and his associates in 1942. The latter authors were able to find five additional nonoperative cases in the literature. Since the publication of this report three additional cases⁴ have been published in which a cure has followed operative treatment. The following report makes a total

of 10 cases thus far reported; it is the sixth case in which a cure has followed operation, and the first in which a lateral suture of the fistula was done.

REPORT OF A CASE

History.—A 46-year-old white factory workman was admitted to the hospital June 6, 1950. He stated that 15 years previously, during an altercation with a barber, he had been stabbed in the left infraclavicular area with a barber shears. Profuse hemorrhage followed, which was controlled by pressure. He recovered rapidly but soon became aware of a diffuse thrill over the entire left infraclavicular area. Except for dyspnea and tachycardia on strenuous exertion, the patient had had no symptoms referable to the injury.

The present illness began three months before admission, when he had "influenza" with generalized aching, chills, and fever. Improvement followed after about 10 days, but five weeks later "virus pneumonia" with recurrence of chills and fever developed. Improvement again occurred after about two weeks, but the patient's appetite was poor; he steadily lost weight and was weak and unable to work. An exacerbation of his symptoms accompanied by shaking chills and profuse sweats led to his admission to the hospital.

Physical Examination.—The patient was acutely ill, with a temperature elevation to 101 F. A healed scar, 1.5 cm. long, was present just below the middle of the left clavicle. A distinct thrill was present in the area of the scar, and a loud machinery murmur was heard over the entire left infraclavicular area. This was also heard over the base of the heart and the left scapular area, and it was transmitted upward in the neck and down the left arm to the antecubital fossa. The left arm was not larger than the right, and the veins were not distended. A good radial

From the Surgical Department, Charles S. Wilson Memorial Hospital, Johnson City, N. Y.

1. Friedberg, C. K.: *Diseases of the Heart*, Philadelphia, W. B. Saunders Co., 1949, p. 778.

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4. (a) Lipton, S., and Miller, H.: Streptococcus Viridans Septicemia—Subacute Bacterial Endarteritis of an Arteriovenous Aneurysm, *J. A. M. A.* 126: 766 (Nov. 18) 1944. (b) Shumacker, H. B., Jr.; Welford, N. T., and Carter, K. L.: Streptococcus Viridans Septicemia from Vegetations in Femoral Arteriovenous Aneurysm: Report of a Case Cured by Surgical Excision of Aneurysm, *Ann. Surg.* 124: 123, 1946. (c) Statland, M., and Orr, T. G.: Streptococcus Viridans Endarteritis of an Arteriovenous Aneurysm, *J. Lab. & Clin. Med.* 34: 221, 1949.

pulse was present, and the blood pressure was approximately the same in both arms. The thrill could be obliterated by pressure, and this was not followed by slowing of the pulse (negative Brannan's sign). No definite heart murmur was present; the lungs were clear; the liver was enlarged one to two fingerbreadths below the costal margin; the spleen was palpable; no petechiae were present.

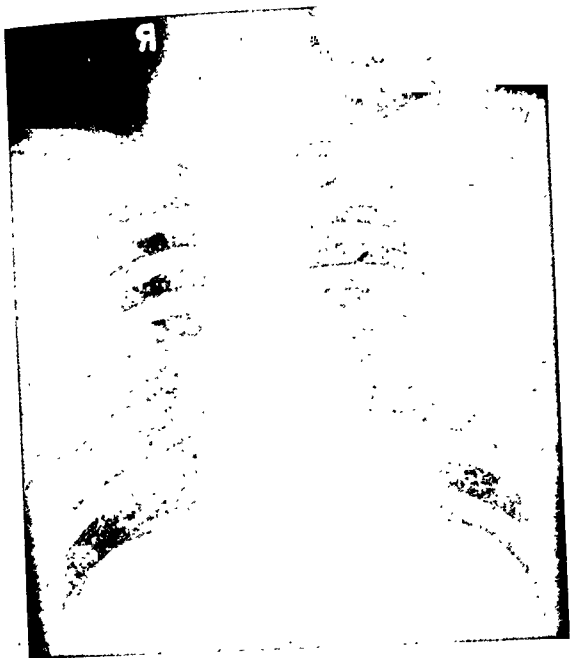


Fig. 1.—This chest roentgenogram was exposed two days after the patient's admission to the hospital. The infiltration in the left lung is believed to be a pulmonary infarct produced by an embolus having its origin in the arteriovenous aneurysm.

Laboratory Data.—The chest roentgenogram demonstrated a calcific plaque in the region of the scar in the left infraclavicular area. The heart was approximately normal in size, and an area of consolidation, probably due to a pulmonary infarct, was present in the left lung (Fig. 1). A blood cell count demonstrated 5,200 leukocytes with 62% neutrophils; the red blood cell count was 4,200,000 and the hemoglobin 11.5 gm., or 74%. Two blood cultures, the first obtained the day following admission and the second taken two days later, yielded a heavy growth of hemolytic streptococci after four days' incubation. Sensitivity of the organism to penicillin and chloramphenicol was determined. It was found that its growth was inhibited by 2 units per cubic centimeter of the former and by 4 γ per cubic centimeter of the latter antibiotic. Numerous additional blood cultures obtained after penicillin therapy was started were all sterile.

Diagnosis and Therapy.—The presence of septicemia with clear-cut evidence of arteriovenous fistula, the absence of a history of rheumatic fever, and the lack of evidence of cardiovascular disease appeared to establish a diagnosis of endarteritis at the site of the arteriovenous communication. Intensive penicillin therapy was started on the day of admission. Two intramuscular injections of 350,000 units and two intravenous doses of 100,000 units were administered daily (a total of 900,000 units). This was continued for a period of 16 days, after which the dosage was reduced to 300,000 units intramuscularly and 100,000 units intravenously. The administration of penicillin in this dosage was continued up to the time of the operation.

Operation.—Intratracheal ether-oxygen anesthesia was administered at operation on June 29. A left thoracocervical⁶ incision was used with resection of a segment of the medial end of the left clavicle and extension to the left axilla. Proximal control of the subclavian artery at the arch of the aorta and of the subclavian vein at its junction with the innominate was obtained. The axillary artery and vein were isolated at the lateral border of the pectoralis major muscle. Control of the shunt was incomplete, and it was necessary to isolate the subclavian vessels again at the level of the first rib, where they were embedded in extra-

ordinarily dense scar tissue. An aneurysm sac measuring 2 by 3 cm. was isolated at the junction of the third portion of the subclavian with the axillary vessels.

The clinical data (good pulse and blood pressure in the left arm, absence of venous distention, and loud murmur, together with the fact that the shunt was readily obliterated at operation by pressure) made it appear practical to attempt a lateral suture of the defect. The vein was accordingly ligated and transfixed with 2-0 cotton sutures 3 cm. proximal and distal to the aneurysm. The artery was controlled at the same level with rubber catheters, after which the vein was divided immediately above and below the aneurysm. The aneurysm was then widely opened, and inspection demonstrated numerous warty 1 to 2 mm. vegetations identical in appearance to those found in instances of rheumatic endocarditis. These were present in the form of a narrow collar exactly at the margin of the defect in the artery. The aneurysm was trimmed almost flush with the artery, and the defect in the latter was closed with three mattress sutures of 4-0 silk mounted on an atraumatic needle. The sutures were applied to the area bearing the vegetations. The suture line was reinforced with the cuff of the aneurysm with similar suture material (Fig. 2).

The wound was then closed with cotton and wire suture material; drainage of the pleural space was provided by two catheters connected to a conventional water seal deflation system. During the operation 2,500 cc. of blood was administered.

Pathologic Examination.⁷—Grossly the specimen was a soft irregular mass of red-brown glistening tissue, 2.5 cm. in its greatest dimension. Microscopically it consisted of hemorrhagic fibroadipose tissue continuous with a large segment of blood vessel wall. Immediately adjacent to the focally ulcerated intima of this structure (but not connected in the sections studied) was a mass of layered fibrin throughout which were dispersed erythro-

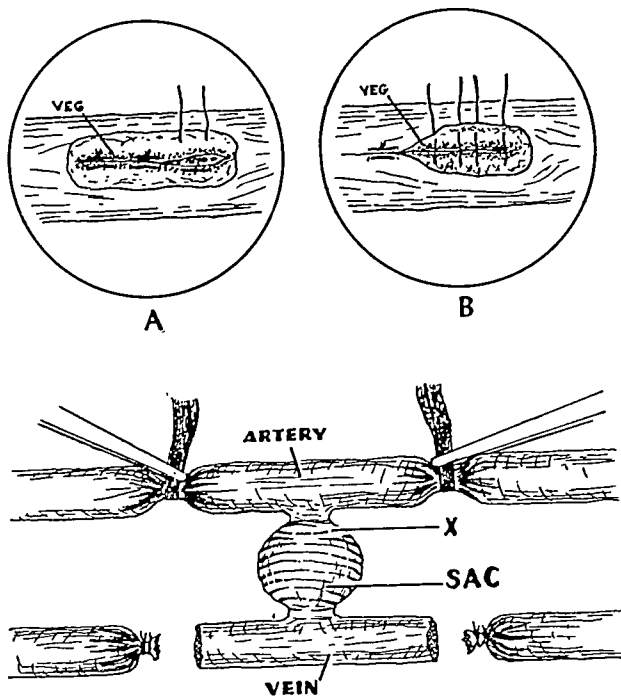


Fig. 2.—This drawing illustrates the aneurysm found at operation. The sac was divided at X, and lateral suture of the defect was done as indicated in insert A and B. The sutures were applied to the area bearing the vegetations.

cytes in varying stages of preservation, with large numbers of neutrophils, the latter arranged diffusely and in clusters. Focal necrosis was prominent. There were basophilic clumps, which

5. Deleted in proof.

6. Williams, M. H.: Accidental Incision of Aneurysm of the Left Common Carotid Artery; Treatment by Thoracocervical Excision with Recovery, *Ann. Surg.*, to be published.

7. Dr. Alexander A. Kosinski, pathologist, C. S. Wilson Memorial Hospital.

probably represented bacterial colonies. There was no evidence of organization.

Postoperative Course.—The patient tolerated the procedure rather well. A small but definite pulse was present immediately after operation, and within a week the left radial pulse was equal to the right. The left lung expanded promptly, and the catheters were withdrawn after 48 hours. Considerable firm swelling of the left arm developed, and this was controlled by elevation of this extremity. Pain over the sternum was severe for about one week. Anticoagulants were not used; penicillin and streptomycin in ordinary dosage were administered for a period of two weeks following operation.

In a small area at the lower angle of the wound the circulation was poor and a superficial slough of skin, measuring 1 by 3 cm., occurred; the remainder of the wound healed by primary union.

Subsequent Course.—The patient was discharged from the hospital July 23, 1950. Six weeks later he returned to his former job in a factory and worked continuously up to Feb. 26, 1951.

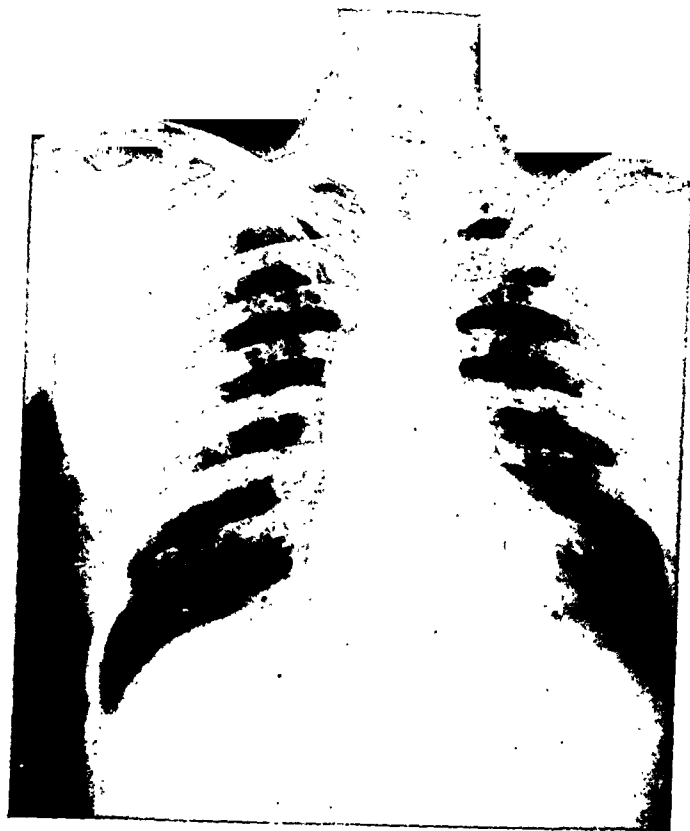


Fig. 3.—This roentgenogram was exposed seven months after operation. The medial third of the clavicle has been resected. The heart appears somewhat smaller as compared with preoperative study (Fig. 1).

During this time partial regeneration of the resected clavicle occurred, producing disability of the left arm in full abduction. Some swelling of the left arm persisted; the circulation remained excellent. The medial end of the clavicle was resected February 28. The patient is now well and has no disability in this extremity. A recent chest roentgenogram (Fig. 3) demonstrates that the heart is now slightly smaller than before the operation.

8. (a) Friedberg,¹ Rienhoff and Hamman,² (b) Touroff, A. S. W., and Vessell, H.: Experiences in the Surgical Treatment of Subacute Streptococcus Viridans Endarteritis Complicating Patent Ductus Arteriosus, *J. Thoracic Surg.* 10:59, 1940. (c) Libman, E.: Discussion of Touroff, A. S. W., The Results of Surgical Treatment of Patency of the Ductus Arteriosus Complicated by Subacute Bacterial Endarteritis, *Am. Heart J.* 25:208, 1943. (d) Taussig, H. B.: Congenital Malformations of the Heart, New York, The Commonwealth Fund, 1947, p. 346.

9. Rienhoff and Hamman,² Touroff, Lande, and Kroop,³ Statland and Orr.^{4c}

10. Rienhoff and Hamman,² Touroff, Lande, and Kroop,³ Lipton and Miller,^{1a} Shumacker, Welford, and Carter.^{1b}

11. The successful result which followed the excision of the infected arteriovenous aneurysm reported by Rienhoff and Hamman² provided the background for the initial attempt^{1b} to cure the septicemia associated with ductus arteriosus by ligation.

COMMENT

The mechanism whereby an arteriovenous shunt predisposes to endocarditis or endarteritis has already received detailed consideration.⁸ It appears that the most important factor is the unequal pressures in the two vessels. This permits arterial blood to flow across the shunt with sufficient force to produce constant trauma to the vein and aneurysm. Arteriosclerotic changes are commonly the end-result of this process. Such changes have been encountered in three of the five operative cases previously reported.⁹ The injury to the aneurysm or vein produces an area favorable for the lodgement and growth of the organisms, which from time to time may gain entry to the blood stream. Because transient bacteremia with *Streptococcus viridans* following various infections or even teeth extraction is of common occurrence, this organism is the usual cause of septicemia in the patients under discussion. In four¹⁰ of the other five operative cases previously reported, this organism was isolated from blood cultures. The organism isolated from the patient of Statland and Orr^{4c} was *Streptococcus mitis*; as previously noted a hemolytic *Streptococcus* was isolated from the patient reported here.

A measure of the resistance of arteriovenous aneurysms and fistulas to infections of this type is attested to by their rarity as compared with the frequent occurrence of such infections in examples of patent ductus arteriosus and interventricular septal defects. It is noteworthy that the aneurysm was of long standing in each of the five operative cases already cited. Among these patients the average duration of the injury before septicemia developed was 10.8 years. As previously noted the patient described here had had his fistulas 15 years.

Antibiotic therapy has become an important aid in the management of patients with endarteritis and septicemia. Among the five cases previously reported, the blood cultures were rendered sterile in two by the preoperative administration of penicillin. This result was also obtained in the case reported here. Quadruple ligation and excision of the aneurysm was done in all of the previously published cases. Lateral suture of the defect without actual removal of the source of the infection effected a cure in the patient described in this report. This result might have been obtained without antibiotic therapy. This statement is supported by the numerous examples of "prepenicillin" cures of septicemia which have been obtained by ligation of a patent ductus arteriosus.¹¹

In general it can be said that penicillin is highly effective in rendering sterile the blood of patients having an arteriovenous aneurysm and septicemia. For this reason it is an important aid in preparing the patient for surgery. Lasting benefits require a proper operation. It is of interest that vegetations were found in the aneurysms of all of the three cases thus far reported in which the blood had been rendered sterile by penicillin.

SUMMARY

A patient with hemolytic streptococcal septicemia associated with a traumatic arteriovenous aneurysm at the junction of the left subclavian and axillary arteries is described. Recovery followed intensive penicillin therapy and lateral suture of the aneurysm.

ADDISON'S DISEASE DUE TO METASTATIC BRONCHOGENIC CARCINOMA

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and

William B. Scharfman, M.D., Jamaica, Long Island, N. Y.

The frequency of adrenal involvement in bronchogenic carcinoma has been noted by many observers. In Willis¹ series of 500 consecutive cancer necropsies, the most frequent adrenal metastases occurred in bronchogenic carcinoma, the incidence being 44%. In contrast, the incidence of adrenal involvement by all cancers was 1%. Willis¹ cited five additional series of bronchogenic carcinomas in which the incidence of adrenal metastases varied from 30% to 40%. In most cases, these metastases were bilateral and situated in the medulla. Jaffe² and Koletsky³ reported the incidence of adrenal involvement as 40% and 45%, respectively; the glandular type of carcinoma was most often responsible.

Koletsky's³ series of 100 bronchogenic carcinomas comprised 10% of all cancers found by him at autopsy. At Queens General Hospital, bronchogenic carcinoma is a frequently encountered malignant tumor; it was found in 2.2% of all autopsies (5,030) performed here during the 10-year period 1936-1945.⁴ The incidence of adrenal involvement in these cases is 44%, occurring in one-fourth of the squamous cell cancers and in about one-half of the oat cell and glandular carcinomas.

In view of the frequency of adrenal involvement just noted, it is most interesting that clinical Addison's disease due to metastatic carcinoma is extremely rare. This may be due to several factors: 1. Incomplete adrenal replacement. In a series of cases of Addison's disease studied at autopsy, less than 5% residual adrenal cortical tissue was found.⁵ 2. Early death due to the primary carcinoma. 3. Metastatic lesions involving primarily the medulla of the adrenal gland.¹

The rarity of Addison's disease due to metastatic involvement of the adrenals is well demonstrated by several series of collected cases. In Guttman's⁶ review of 566 cases reported up to 1930, tuberculosis was the most frequent cause of Addison's disease, with primary atrophy an important but less common etiologic mechanism; only two primary neoplasms and three metastatic tumors were included. He apparently does not accept the four cases attributed to metastatic carcinoma by Philpott,⁷ none of which was described. Sorkin's⁸ series of 25 cases studied post mortem included no case due to neoplasm. Soffer⁹ cites Rowntree and Snell's series of 31 cases, Snell's series of 30 cases, Duffin's series of 17 cases, and his own 12 cases, all found at autopsy, none of which demonstrated neoplastic adrenal involvement as the etiologic factor. The standard textbooks dealing with Addison's disease mention metastatic adrenal involvement as a rare etiologic factor; however, their only documentation refers to Guttman's review of 1930.

A review of Addison's¹⁰ original 11 cases, of which four were attributed to metastatic carcinoma (from breast, stomach, uterus, and lung), shows that these cases presented an equivocal clinical picture, with limited or no history given in all four cases. Post-mortem studies of these four cases showed only unilateral adrenal involvement.

We concur with Soffer's⁹ opinion that "it would seem very doubtful that any of this group were true instances of Addison's disease."

Goldzieher¹¹ states that only a few cases of clinically unquestionable Addison's disease due to tumors are on record (Foersterling, Hertz and Secher, Packard and Steele, Bannwart).

In the American literature, we have been unable to find any confirmed case report of Addison's disease due to replacement of adrenal tissue by tumor. In 1924, Warthin and co-workers¹² reported a case of pigmentation of the skin (Addison's disease) associated with lymphosarcoma involving the lymph nodes of the solar plexus region. However, at autopsy, the adrenals were moderately atrophic with minimal lymphosarcomatous infiltration. Similarly, in the British literature, Bicknell¹³ reported a case of skin pigmentation in a man with gastric metastases in abdominal lymph nodes pressing on the solar plexus; the adrenals were normal at autopsy.

Poynton and co-workers¹⁴ reported two cases of bronchogenic carcinoma with cough, weakness, anorexia, and weight loss, in one of which skin pigmentation developed. At autopsy, this case grossly showed residual adrenal cortical tissue. The second case showed tumor only in the left adrenal, the right appearing normal.

In 1942, Strang¹⁵ described a man with skin pigmentation, bouts of weakness, anorexia, asthenia, vomiting, and hypotension. Autopsy showed bronchogenic carcinoma (oat cell type) with replacement of both adrenals by metastases.

From the Department of Pathology (Alfred Angrist, M.D., Director) and the Department of Medicine (James R. Reuling, M.D., Director) Queens General Hospital, Jamaica, N. Y.

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12. Warthin, A. S.; Crane, A. W., and Jackson, J. B.: Pigmentation of the Skin (Addison's Disease) Associated with Lymphosarcoma Involving Particularly the Retroperitoneal Lymph Nodes of the Solar Plexus Region, *Arch. Dermat. & Syph.* 10: 139 (Aug.) 1924.

13. Bicknell, F.: Addison's Disease Due to Malignant Involvement of the Solar Plexus, *Brit. M. J.* 2: 206 (Aug. 4) 1934.

14. Poynton, F. J.; Wright, G. P., and Laurent, L. P. E.: Clinical Symptoms of Addison's Disease Occurring in the Course of Pulmonary Carcinoma, *Lancet* 1: 740 (April 8) 1933.

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REPORT OF A CASE

The following case report¹⁶ describes Addison's disease due to adrenal replacement by metastases from a bronchogenic carcinoma.

G. V., a 58-year-old white man, entered Queens General Hospital on Oct. 15, 1948, with complaints of anorexia, weakness, and weight loss. The symptoms began approximately 12 months before entry, when vague indigestion and anorexia were noted. Several visits to local physicians resulted in varying diagnoses such as "nervous stomach" and cholecystitis. Cholecystograms disclosed no abnormalities. One x-ray was interpreted as demonstrating an immovable right diaphragm. Three months before entry the patient's physician noted a hilar mass and a right inguinal mass. The diagnosis from biopsy of the inguinal mass was adenocarcinoma, primary site undetermined. He was given pteropterin® (sodium pteroyl triglutamate) and radiation to the chest. Despite this therapy, asthenia and anorexia increased in severity. He had a 40 lb. (18 kg.) weight loss over a period of about one year. No localizing symptoms referable to the chest, abdomen, or genitourinary tract were elicited. Past history, review of systems, and family history were irrelevant.

Physical examination revealed an emaciated, asthenic man who appeared pale and chronically ill. The temperature was 98.6 F, pulse rate 80, respirations 16, and blood pressure 110/80. The skin contained numerous deeply pigmented spots on the

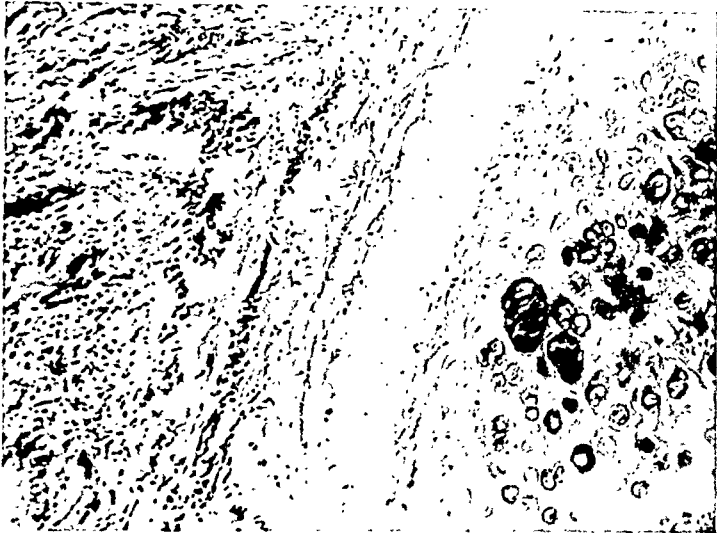


Fig. 1.—Photomicrograph of tissue from the bronchus. This shows primary bronchogenic carcinoma composed of anaplastic, glandular tissue with some scirrhous reaction.

face, arms, chest, and back, which the patient thought he had always had. The mucous membranes were pale but otherwise not remarkable. There was no increased pigmentation in the axillary folds or pressure points. The scalp was normal. The eyes revealed the left pupil smaller than the right, with a sluggish light response on the left. The fundi were not remarkable. The ears, nose, and throat were normal. The neck was supple, with no tracheal deviation, thyroid, or lymph node enlargement. The spine was normal. The chest was symmetrical, with pigmentation over the anterior wall, which corresponded to the site of previous radiation therapy. The lungs revealed no auscultatory or percussion abnormalities. The heart was normal. No organs or masses were palpable in the abdomen. The extremities were normal. A healed scar was present in the right inguinal region, with a hard immovable mass underlying the incision. Superficial and deep tendon reflexes were within normal limits. Rectal examination disclosed no abnormalities. The admitting impression was metastatic carcinoma, primary site undetermined; bronchus, gastrointestinal tract, and pancreas were mentioned as possibilities.

On admission the urine was normal. The white cell count was 11,250, with a normal differential count, red cell count

3,120,000, and hemoglobin 9.5 gm. The fasting blood sugar was 90 mg. per 100 cc. and blood urea nitrogen 20 mg. per 100 cc. The icterus index was 4.0, phosphorus 5.3 mg. per 100 cc., acid phosphatase 0.8 units, alkaline phosphatase 11.7 units, total protein 6.8 gm. per 100 cc. (albumin 4.6 and globulin 2.2).

The patient was treated with a high caloric diet. X-rays on October 21 revealed no bone abnormalities. A chest x-ray showed the trachea to be deviated to the right; a homogeneous density was seen involving the upper portion of the right lung field extending down to the second rib anteriorly. The radiographic appearance was suggestive of a primary Pancoast tumor. Weakness and fatigue persisted. On November 10, 500 cc. of whole blood was given. On December 2, six weeks after entry, increasing pigmentation was noted. Asthenia was marked, and blood pressure was 95/65. At this time, Addison's disease secondary to metastatic involvement of the adrenals was suspected.



Fig. 2.—Photomicrograph of adrenal tissue. This shows complete replacement by anaplastic glandular carcinoma.

On December 7 the blood pressure was 85/60, and the patient had lost 13 lb. (6 kg.) in six weeks. By December 13 the chest x-ray showed no change. On November 22, the plasma chlorides were 96 mEq. per liter; repeat examination on December 2 showed 85 mEq. A Robinson-Kepler-Power test was positive in parts I and II, with A equal to 5.7. Serum potassium was 20.5 mg. per 100 cc. The serum sodium was 122 mEq. per liter (281 mg. per 100 cc.). A glucose tolerance test showed a mild diabetic curve (fasting sugar 100, maximum 225 mg. per 100 cc., and 165 mg. per 100 cc. after three hours). On December 10, desoxycorticosterone therapy (5 mg. intramuscularly every second day) with enteric-coated sodium chloride (5 gm. daily) was instituted. Despite therapy a watery diarrhea persisted. On December 20, 10 days after therapy was begun, the blood pressure had risen to 108/68 and the patient had gained 5 lb. (2.5 kg.). On December 23, the 17-ketosteroids were 4.34 mg. in 24 hours. On December 26, pulmonary edema suddenly developed and the patient died the following day. The clinical diagnoses were carcinomatosis,

16. This case will be included in the series to be published from this hospital by Butterly, J. M.; Fishman, L.; Seckler, J., and Steinberg, H.: Addison's Disease Secondary to Metastatic Carcinoma of the Adrenal Glands.

probable primary site in the bronchus, Addison's disease secondary to adrenal metastases, and acute pulmonary edema.

At autopsy, the skin contained multiple freckles, which varied from dark brown to black. Diffuse brown pigmentation was present on the face and both arms. There was a tumor arising from the right upper lobe bronchus and involving almost the entire upper lobe parenchyma (Fig. 1). Both adrenal glands were completely replaced by tumor tissue, no recognizable adrenal parenchyma remaining. Tumor involvement of the subcutaneous lymph nodes was present in the inguinal, cervical, and axillary regions. There was also tumor involvement of the submucosa of the jejunum. Microscopic examination of the tissues showed the tumor to be an adenocarcinoma. The adrenals were completely replaced by tumor, with no residual glandular tissue seen (Fig. 2). The final anatomic diagnosis was bronchogenic adenocarcinoma, right upper lobe, with metastases to both adrenals, jejunum, and subcutaneous lymph nodes, and pulmonary edema.

COMMENT

It is felt that the above case represents true Addison's disease confirmed by clinical history and physical examination, complete laboratory study, response to therapy, and autopsy showing complete replacement of the adrenal glands. In the absence of any diabetic pathological changes in the pancreas or kidney, and considering the normal fasting blood sugar, we are unable to explain the moderate elevation and prolongation of the blood sugar levels in the glucose tolerance test.

Some of the reasons for the rarity of this condition have been discussed, namely, incomplete adrenal replacement, early death from the primary disease, and involvement chiefly of the medulla by metastatic lesions. In addition, failure to suspect this possibility clinically is an important reason. This may be due to the absence of previous reports as well as to some similarities in the symptoms of advanced carcinoma and Addison's disease, in particular anorexia, weakness, asthenia, and weight loss.

SUMMARY AND CONCLUSIONS

A case of Addison's disease due to adrenal replacement by metastases from bronchogenic carcinoma is reported. Addison's disease due to metastatic tumor replacing the adrenals is an extremely rare condition. Review of the American literature fails to disclose any acceptable cases of this entity, and a paucity of cases is noted in the foreign literature. The probable explanations for the infrequency of this syndrome is discussed.

Cranks and Scientists.—There is hardly a scientific theory that is not questioned by some scientist of repute. This is so because science is unfinished business, an inquiry into the habits of nature where all the evidence is not in and where much of the evidence that is in has not been digested. Under these conditions there is room for minority opinions, some of which will, no doubt, turn out to be correct. There is a parallel here, though, with horse racing: long shots run in the races, and some will no doubt win. But a sports commentator who expected a long shot to win in almost every race would be open to suspicion. In the same way, the man who accepts one or two scientific "long shots" is perfectly reasonable, but when a man accepts too many of them, his scientific standing becomes suspect. The crank is one who tries to force nature into his own selected pattern; the evidence of strain resulting from this practice is divergence from currently accepted views. In attempting to defend these divergences, the crank may be led to excessive reliance upon minority opinions and the authority of individuals. As a corollary to this, he may also attempt to discredit majority opinion, scientific method, or scientists in general.—Laurence J. Lalleur, *Cranks and Scientists*, *The Scientific Monthly*, November, 1951.

CLINICAL NOTES

TELOGNOSIS

THREE YEARS OF EXPERIENCE WITH DIAGNOSIS BY TELEPHONE-TRANSMITTED ROENTGENOGRAMS

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H. S. Read, M.D.

Bernard Caplan, M.D., Atlantic City, N. J.

and

A. G. Cooley, New York

Telognosis, or the interpretation of facsimile roentgenograms obtained from distant sources by telephone or radio,¹ has been used continuously since 1947. Fol-

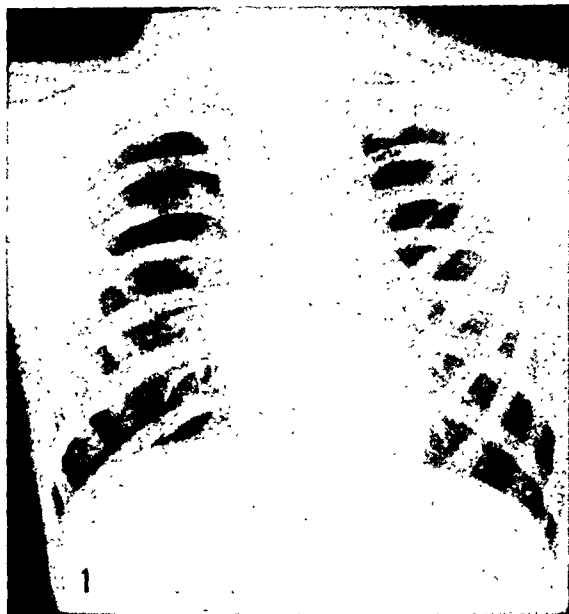


Fig. 1.—Facsimile of a chest roentgenogram of a 6-year-old boy transmitted over a telephone circuit 60 miles long.

lowing the initial trial of this system between Chester County Hospital, West Chester, Pa., and Philadelphia, a circuit was established over busy commercial telephone channels between the Ventnor Clinic in Atlantic City, N. J., and Philadelphia, a distance of 60 miles (100 km.). This circuit has been tested continuously during the past year to determine whether a full-time roentgenologic service could be maintained, and to explore this method of teaching radiologists in training.

The apparatus consists of a transmitter that scans roentgenograms of any size up to 14 by 17 in. (35.6 by 43.2 cm.). The receiver reproduces facsimiles reduced to half the size of the original films. Consultations and

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1. Gershon-Cohen, J., and Cooley, A. G.: Roentgenographic Facsimile: A Rapid Accurate Method for Reproducing Roentgenograms at a Distance via Wire or Radio Transmission, *Am. J. Roentgenol.* 61:557-559 (April) 1949; *Telognosis*, *Radiology* 55:582-587 (Oct.) 1950.

REPORT OF A CASE

The following case report¹⁶ describes Addison's disease due to adrenal replacement by metastases from a bronchogenic carcinoma.

G. V., a 58-year-old white man, entered Queens General Hospital on Oct. 15, 1948, with complaints of anorexia, weakness, and weight loss. The symptoms began approximately 12 months before entry, when vague indigestion and anorexia were noted. Several visits to local physicians resulted in varying diagnoses such as "nervous stomach" and cholecystitis. Cholecystograms disclosed no abnormalities. One x-ray was interpreted as demonstrating an immovable right diaphragm. Three months before entry the patient's physician noted a hilar mass and a right inguinal mass. The diagnosis from biopsy of the inguinal mass was adenocarcinoma, primary site undetermined. He was given pteropterin® (sodium pteroyl triglutamate) and radiation to the chest. Despite this therapy, asthenia and anorexia increased in severity. He had a 40 lb. (18 kg.) weight loss over a period of about one year. No localizing symptoms referable to the chest, abdomen, or genitourinary tract were elicited. Past history, review of systems, and family history were irrelevant.

Physical examination revealed an emaciated, asthenic man who appeared pale and chronically ill. The temperature was 98.6 F, pulse rate 80, respirations 16, and blood pressure 110/80. The skin contained numerous deeply pigmented spots on the

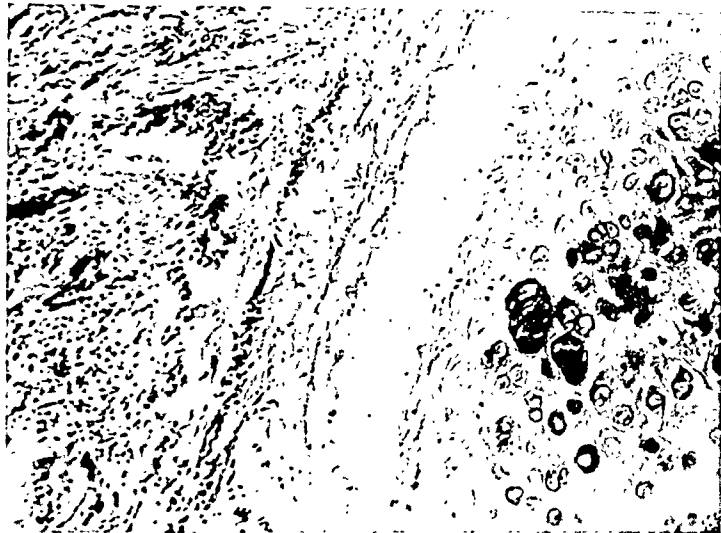


Fig. 1.—Photomicrograph of tissue from the bronchus. This shows primary bronchogenic carcinoma composed of anaplastic, glandular tissue with some scirrhus reaction.

face, arms, chest, and back, which the patient thought he had always had. The mucous membranes were pale but otherwise not remarkable. There was no increased pigmentation in the axillary folds or pressure points. The scalp was normal. The eyes revealed the left pupil smaller than the right, with a sluggish light response on the left. The fundi were not remarkable. The ears, nose, and throat were normal. The neck was supple, with no tracheal deviation, thyroid, or lymph node enlargement.

The spine was normal. The chest was symmetrical, with pigmentation over the anterior wall, which corresponded to the site of radiation therapy. The lungs revealed no auscultatory or percussion abnormalities. The heart was normal. No organs or masses were palpable in the abdomen. The extremities were normal. A healed scar was present in the right inguinal region, with a hard immovable mass underlying the incision. Superficial and deep tendon reflexes were within normal limits. Rectal examination disclosed no abnormalities. The admitting impression was metastatic carcinoma, primary site undetermined; bronchus, gastrointestinal tract, and pancreas were mentioned as possibilities.

On admission the urine was normal. The white cell count was 11,250, with a normal differential count, red cell count

3,120,000, and hemoglobin 9.5 gm. The fasting blood sugar was 90 mg. per 100 cc. and blood urea nitrogen 20 mg. per 100 cc. The icterus index was 4.0, phosphorus 5.3 mg. per 100 cc., acid phosphatase 0.8 units, alkaline phosphatase 11.7 units, total protein 6.8 gm. per 100 cc. (albumin 4.6 and globulin 2.2).

The patient was treated with a high caloric diet. X-rays on October 21 revealed no bone abnormalities. A chest x-ray showed the trachea to be deviated to the right; a homogeneous density was seen involving the upper portion of the right lung field extending down to the second rib anteriorly. The radiographic appearance was suggestive of a primary Pancoast tumor. Weakness and fatigue persisted. On November 10, 500 cc. of whole blood was given. On December 2, six weeks after entry, increasing pigmentation was noted. Asthenia was marked, and blood pressure was 95/65. At this time, Addison's disease secondary to metastatic involvement of the adrenals was suspected.

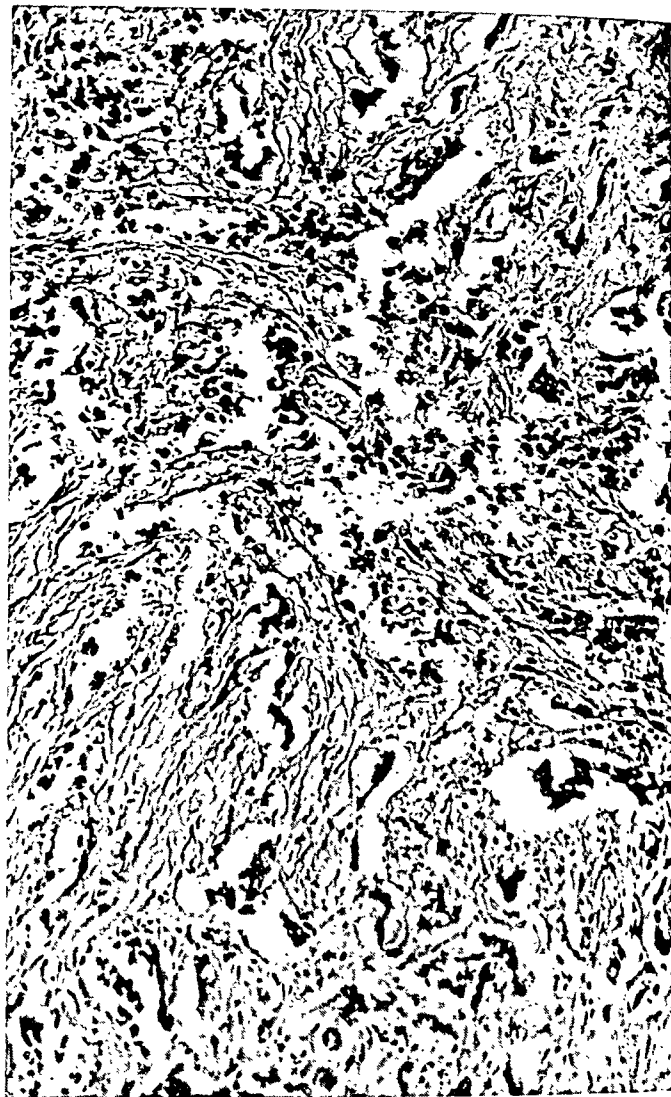


Fig. 2.—Photomicrograph of adrenal tissue. This shows complete replacement by anaplastic glandular carcinoma.

On December 7 the blood pressure was 85/60, and the patient had lost 13 lb. (6 kg.) in six weeks. By December 13 the chest x-ray showed no change. On November 22, the plasma chlorides were 96 mEq. per liter; repeat examination on December 2 showed 85 mEq. A Robinson-Kepler-Power test was positive in parts I and II, with A equal to 5.7. Serum potassium was 20.5 mg. per 100 cc. The serum sodium was 122 mEq. per liter (281 mg. per 100 cc.). A glucose tolerance test showed a mild diabetic curve (fasting sugar 100, maximum 225 mg. per 100 cc., and 165 mg. per 100 cc. after three hours). On December 10, desoxycorticosterone therapy (5 mg. intramuscularly every second day) with enteric-coated sodium chloride (5 gm. daily) was instituted. Despite therapy a watery diarrhea persisted. On December 20, 10 days after therapy was begun, the blood pressure had risen to 108/68 and the patient had gained 5 lb. (2.5 kg.). On December 23, the 17-ketosteroids were 4.34 mg. in 24 hours. On December 26, pulmonary edema suddenly developed and the patient died the following day. The clinical diagnoses were carcinomatosis,

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condition rests with the physician who sees the newborn during the first 15 minutes of life. The condition may be suspected when it is impossible to get the baby "dry" in spite of repeated aspirations of saliva and mucus from the mouth. Excessive salivation and a frothy mucus continues to occur at the mouth of an infant so affected.

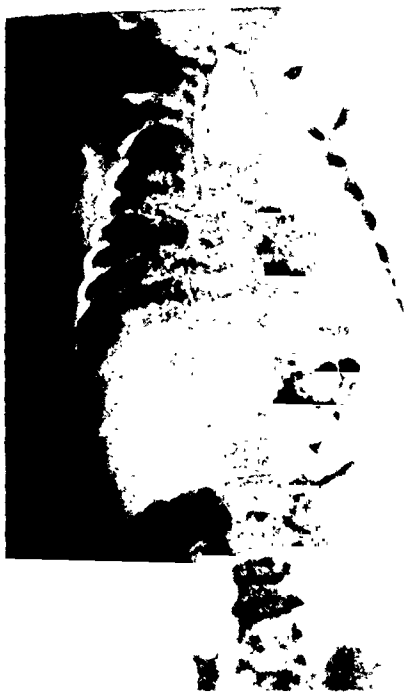


Fig. 1.—Roentgenogram of the infant one hour old, confirming the initial diagnosis of tracheoesophageal fistula.

When this picture is present, a no. 8 or 10 French catheter should be passed gently, while the baby is yet in the delivery room, through the oropharynx into the esophagus until a point of obstruction is encountered. Prompt roentgenographic studies should follow, which either rule out or definitely establish the presence of tracheoesophageal fistula. With the diagnosis only needing confirmation by means of x-ray studies, the small catheter is reinserted and through it 2 to 3 cc. of iodized oil is instilled into the esophagus while fluoroscopic observation is conducted. The various types of tracheoesophageal fistulas are readily recognized in the roentgenograms and have been conveniently classified into five types by Ladd.

Once early diagnosis is made, immediate surgery is indicated. In those cases in which the diagnosis is established before the baby is more than a few hours old, there has not, as a rule, been time for pneumonitis, which invariably complicates the condition, to develop. The resistance of the infant and the state of hydration are such that surgery can be performed with the least risk and a minimum of replacement and supportive therapy. In situations in which a primary end-to-end anastomosis of the esophagus can be accomplished, it is unnecessary to do a preliminary or even subsequent gastrostomy. Sufficient clydes during the first 48 hours postoperatively can be given to assure adequate intake and maintenance of necessary metabolic requirements. The infant's "dry mouth" postoperatively is in sharp contrast to the situation prior to surgery. When the "dry mouth" is seen, one

can feel certain that the esophagus is patent, but again, fluoroscopic and roentgenographic confirmation, with the use of iodized oil, is indicated. With a patent esophagus assured, oral feedings are begun and gradually increased over a period of two weeks. At the end of this time normal formula requirements can be met.

The following report exemplifies the value of early diagnosis and prompt surgery in a case of tracheoesophageal fistula.

REPORT OF A CASE

On June 6, 1950, at 5:37 p. m., a 7 lb. 10¼ oz. (3,480 gm.) baby girl was born. The mother, a 23-year-old primipara, was delivered by low forceps episiotomy under general anesthesia after an uncomplicated pregnancy. The delivery was without incident other than the fact that the newborn presented with excessive amounts of saliva and frothy mucus at the mouth. A small hemangioma of the face was also noted. The attending staff suspected tracheoesophageal fistula in this infant. While the infant was still in the delivery room, a no. 8 French catheter was inserted into the esophagus but seemed to meet an obstruction. The next step was to confirm the diagnosis by x-ray studies. Between 6:30 p. m. and 7:30 p. m. fluoroscopy and roentgenography were accomplished by the hospital roentgenologist. Three cubic centimeters of iodized oil was instilled through a no. 8 French catheter into the proximal esophagus. A Type III tracheoesophageal fistula, as described by Ladd, was visualized (fig. 1) without difficulty and the surgeon (C. J. M.) notified. The case was reviewed, and all consultants agreed to immediate surgery. The infant could be in no better condition with such an anomaly than at the time. The anesthesiologist was notified and operating room made ready; at 11:45 p. m. the anesthetic was begun. The patient was just over 6 hours old.

Under general ether anesthesia, the infant was placed on her left side and the right side and back prepared with ether and draped in the usual fashion. A hockey-stick type of incision was made medial and inferolateral to the elevated scapula for exposure of the second, third, and fourth ribs. The proximal 6 cm.

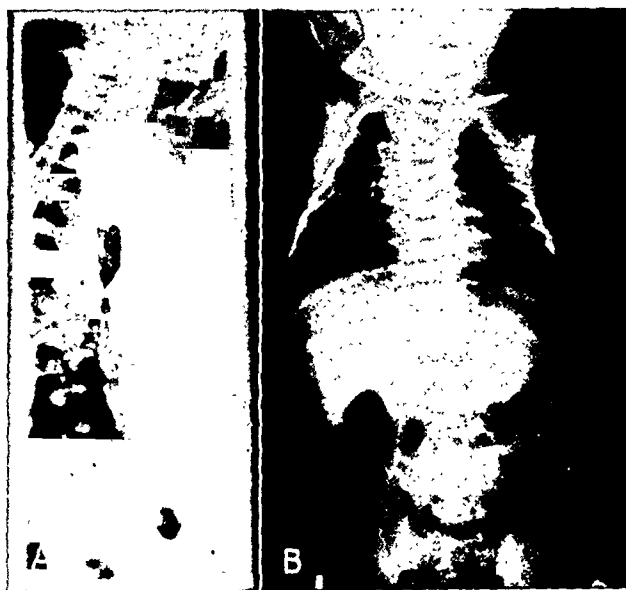


Fig. 2.—A, roentgenogram of infant 36 hours postoperatively, illustrating patency of esophagus. Narrowing at suture line is due largely to edema. B, roentgenogram of patient at 3 weeks of age. Clinically the child was well and presented no evidence of esophageal or pulmonary disease.

of these ribs was resected just beyond their neck and the parietal pleura reflected inferiorly and anteriorly. Care was taken to remain extrapleural. When the azygos vein was divided, the tracheoesophageal fistula could be visualized without difficulty. The distal part of the esophagus was found to stem from a point

0.5 cm. above the bifurcation of the trachea. A no. 00 black silk ligature was carefully tied close to the trachea and the esophagus divided. When the proximal esophageal pouch was freed, it was then possible to accomplish an open end-to-end anastomosis of the esophagus between the pouch above and the distal esophagus below, using no. 00000 atraumatic black silk sutures. There was no evidence of leakage on completion of the anastomosis. The right lung was reexpanded with positive pressure anesthesia. The wound was closed in layers with interrupted surgical and black silk sutures. A firm dressing was applied to the wound, and the infant was returned to its incubator. The entire operative procedure was performed in two hours. The patient was given penicillin, 20,000 units every three hours; streptomycin, 0.12 gm. every six hours; nothing by mouth; continuous oxygen; and suction of oral contents as necessary. Within the first 24 hours, in addition to the above, 30 cc. of 5% glucose in isotonic sodium chloride solution and 90 cc. of 5% glucose in distilled water were given by clysis. During the next 12 hours, 50 cc. of 5% glucose in isotonic sodium chloride solution and 10 mg. of a water-soluble, synthetic vitamin K compound (synkayvite®) were given. Thirty-six hours postoperatively the patient was sent to the x-ray department for study with iodized oil (3 cc. orally). When this material was seen to pass without difficulty (fig. 2A), feedings of sterile water (4 cc.) every two hours were begun for 36 hours. Following this, feeding with similac® (8 cc.) was begun. Feedings were gradually increased over a two-week period so that normal oral formula intake could be met. The infant's temperature was at its peak the day of surgery (100.8 F) and gradually subsided to normal over a one-week period. One week after surgery the patient had lost 7¼ oz. (206 gm.), and at the beginning of the second week she was 2 oz. (57 gm.) less than birth weight. At the beginning of the third week the infant had regained her birth weight.

The patient's clinical course was exceptionally smooth. Skin sutures were removed on the sixth postoperative day. A slight edema of the eyelids was present a few days postoperatively, owing to the irritation from open ether anesthesia. The hematologic picture was within normal limits as regards red cell count and hemoglobin. The white cell count and differential count remained elevated until one week postoperatively, at which time it returned to normal limits. Roentgenograms (fig. 2B) the day prior to discharge revealed clear lung fields with no residual pneumonitis or iodized oil. Noted incidentally was another congenital anomaly, a bifid third thoracic vertebra. The patient was discharged June 28, when 22 days old, apparently cured.

Although the patient left the city at 6 months of age, correspondence from the family indicates that the child, now over a year old, is progressing well and growing normally.

COMMENT

The diagnosis of tracheoesophageal fistula is incumbent on the first physician to handle the infant, be he general practitioner, obstetrician, or pediatrician. The newborn with excessive salivation and frothy mucus, which continues to appear at the mouth, and is difficult to keep "dry" in spite of repeated aspirations, should be suspected of having such an anomaly. Such suspicion should prompt the cautious passage of a small French catheter. If the tube meets an obstruction, roentgenographic studies with iodized oil in small amounts should be made. When the diagnosis has been thus confirmed, immediate surgery on the newborn is indicated and, when technically possible, ligation of the fistula with primary end-to-end anastomosis of the esophagus should be performed. No gastrostomy and little supportive therapy seems indicated in infants so treated in the first six and possibly twelve hours of life. A case to illustrate these facts is reported.

415 Pujó St. (Dr. Weiss).

CUTANEOUS SEQUELAE FOLLOWING TREATMENT OF BRONCHIAL ASTHMA WITH INORGANIC ARSENIC

REPORT OF TWO CASES

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and

Jack Wolf, M.D., New York

During the fall of 1950 two patients with classical arsenical eruptions were seen at the Skin and Cancer Unit of New York University Hospital. The first had an arsenical melanosis and the second a diffuse and pro-



(Case 1) Arsenical hyperpigmentation of skin following administration of Fowler's solution for treatment of bronchial asthma.

nounced arsenical pigmentation of the skin associated with numerous punctate keratoses on the neck, shoulders, palms, and soles. Both patients gave the history of having taken orally medicament containing Fowler's solution (solution of potassium arsenite) and potassium iodide for more than one year prior to admission for the alleviation of asthma. To our knowledge, a detailed report on this method of treatment has not been published, but a brief description has been recorded.¹ The purpose of this paper is to call attention to the untoward effects attributable to this treatment in two cases.

From the Department of Dermatology and Syphilology, New York University Postgraduate Medical School (Chairman, Dr. Marion B. Sulzberger), and the Skin and Cancer Unit of the University Hospital.

1. The Gay Treatment for Asthma, Queries and Minor Notes, J. A. M. A. 130: 379 (Feb. 9) 1946.

REPORT OF CASES

CASE 1.—J. D., a white man, 58, was admitted on Sept. 5, 1950. He had had asthma and a chronic cough for four years. Two radical sinus operations were performed, and nasal polyps were removed shortly after the onset of these symptoms. Prior to January, 1949, aminophylline suppositories and aminophylline tablets (U. S. P.) and a nasal spray containing ephedrine sulfate were the principal medicaments used for relief. From January, 1949, to April, 1950, the patient took orally medicament which his physician claimed was the same as that supplied by a clinic at Biloxi, Miss. During this 15 month period he was given 20 to 25 bottles (4 oz. [120 gm.] each) of the medicament. The patient was instructed to take 1 teaspoonful three times a day for six consecutive weeks, then 1 teaspoonful twice a day for six months, and then 1 teaspoonful a day for the balance of the period. Because there was no notable improvement, the patient decided to visit the clinic in Biloxi. His first visit to this clinic was on May 5, 1950, at which time he was given a supply of a red liquid, which appeared to him to be identical with the medicament taken previously. He was also instructed to take 1 calcium tablet daily and "doxychol K" (a mixture of ketocholanic acids and desoxycholic acid) to keep his bowel movements regular. After an observation period of one week, the patient returned to his home, where treatment was continued as outlined for two additional weeks. At the end of the third week the patient complained of loss of appetite, loss of weight (approximately 4 or 5 lb. [1.8 to 2.3 kg.]), and some itching. No eruption was noted at the time. The patient reported these symptoms by mail to the clinic in Biloxi, whereupon he was sent a new supply of a red liquid with word that the new red liquid was the same except that the proportion of some of the components had been changed. The patient appeared to tolerate the altered formula well. Approximately 10 oz. (300 gm.) were consumed during May, 6 oz. (180 gm.) during July, and 6 oz. during August, 1950. The episodes of asthma continued to recur nevertheless, and the patient found it necessary to take aminophylline tablets (U. S. P.) or use aminophylline suppositories and an ephedrine nasal spray for the severer attacks. During August, 1950, isopropylarterenol ("norisodrine") sulfate was added to the list of drugs which the patient used for relief. Late in August, two weeks prior to his first visit to the Skin and Cancer Unit, a somewhat pruritic eruption developed for which he came to the Skin and Cancer Unit. He was unaware of any discoloration of the skin.

Physical Findings: The patient was moderately dyspneic and cyanotic. There was a mottled hyperpigmentation of the skin of the neck, chest, upper part of the back, and upper extremities. The oral mucosa and the skin over the face, abdomen, lower part of the back and lower extremities were spared. Superimposed on this hyperpigmented background was a papular erythematous eruption of small red papules uniformly distributed over the chest, abdomen, back, and arms. Other findings of note were an emphysematous chest, dry sibilant bronchi, and enlargement of the right side of the heart.

Laboratory Findings: Histological sections of the hyperpigmented skin of the anterior chest wall were examined by Dr. Charles F. Sims. The essential changes were the presence of pigment in most of the basal cell layers, pigment laden chromatophores, and free pigment granules in the upper corium. A histological diagnosis of "pigmentation (melanin) consistent with the clinical diagnosis of arsenical pigmentation" was made.

Patch tests with the following agents gave negative reactions: 30% potassium iodide in petrolatum, 30% potassium bromide in petrolatum, petrolatum (control), Fowler's solution, "red liquid" taken orally, 1% ephedrine sulfate solution, and isopropylarterenol sulfate. Intracutaneous tests with inhalants and foods elicited no significant immediate wheal reactions.

Repeated routine urinalysis showed no abnormal findings except for a faint trace of protein in some specimens. A test for arsenic in the urine showed 0.7 mg. per 100 cc. in 1,400 cc. (normal is 0 to 1.0 mg. in 24 hours by Gutzeit method, with unrestricted diet). The initial blood count showed 6,000,000 erythrocytes, 17.4 gm. (120%) of hemoglobin, and 6,500 leukocytes per cubic milliliter of blood. The hematocrit reading was 70% (normal is 40 to 45%).

X-ray examination of the sinuses disclosed a pansinusitis, most marked of the antra and ethnoids. Electrocardiographic tracings showed changes compatible with cor pulmonale.

Course: When first seen on Sept. 5, 1950, the patient was advised to discontinue use of all medicaments except the aminophylline preparations for symptomatic relief. The erythematous papular eruption distributed over the chest, abdomen, back, and arms disappeared within 10 days, but there was no change in the nature or degree of hyperpigmentation. On reexamination on July 19, 1951, it was found that the erythematous papular eruption which was present on the initial examination had not recurred. The degree of hyperpigmentation, however, appeared even more pronounced. Questioning revealed that during November, 1950, the patient had resumed the ingestion of the red liquid medicament. Isopropylarterenol sulfate, whose use was introduced prior to the onset of the erythematous papular eruption in August, 1950, was not taken again.

Diagnosis: The diagnosis was bronchial asthma, polycythemia secondary to anoxemia, sinusitis, arsenical pigmentation of the skin, and dermatitis medicamentosa, presumably due to isopropylarterenol sulfate.

CASE 2.—H. S., a white man, 24, first came to the outpatient department of the Skin and Cancer Unit on Oct. 21, 1950, because of an eruption on the hands and feet and a "nail condition" of several months duration. He was unaware of the other cutaneous changes discovered on examination of the skin.

History: The patient had had a "skin condition" from the time of infancy up to the age of 6 years. Bronchial asthma followed soon after this dermatosis healed. During 1945, at the age of 18, a disabling sinusitis also developed. These various "allergic" manifestations influenced him in the selection of his college, and he decided to continue his schooling in Arizona. During the three years in Arizona his health was much improved, and he had relatively few asthmatic attacks. On returning to New York in 1948, he remained comparatively well for about seven to eight months, only to lapse into a status asthmaticus lasting more than two weeks. It was at this time (April, 1949) that he began taking the following arsenic containing prescription:

Fowler's solution.....	8.0 cc.
Potassium iodide.....	6.5 gm.
Phenobarbital.....	0.6 gm.
Saccharin.....	0.5 gm.
Tincture of cudbear.....	1.0 cc.
Distilled water to make a total of.....	60.0 cc.

The patient was informed that the medicament was essentially the Gay formula. In accordance with instructions, 1 teaspoonful of this preparation was taken twice daily until July 20, 1950, a period approximating 15 months. The patient then discontinued use of the medicament and remained free from asthma up to the time of admission. Neither the patient nor his family were able to give any information relative to previous medicaments used beyond the fact that during the patient's entire lifetime he had taken medicament in one form or another.

Physical Examination: The patient showed a mottled dusky gray and rather pronounced hyperpigmentation of the entire integument. This hyperpigmentation was less apparent on the face than on other parts of the body. Only the oral mucosa was spared. In addition, small punctate keratoses were found over the back, shoulders, palms, and soles, more numerous on the palms and soles than in the other areas. The palmar and plantar surfaces also appeared dry, scaly, and somewhat erythematous. The nails of the middle and ring fingers of both hands were partially destroyed, exposing a roughened and thickened floor. The affected nails were broken off close to the cuticle, and the distal edge of each nail was separated from the nail bed underneath.

Laboratory Findings: Two biopsies were performed, one of a hyperpigmented area on the chest and the other of a hyperkeratotic portion of the left sole. The histological examinations were made by Dr. Arthur Hyman, who considered the findings in both sections part of the picture of arsenical intoxication. A mycological examination was made of the affected fingernails, palms, and soles. Candida albicans was cultured from the nails. No fungi or yeasts were recovered from the soles.

Course: There was little or no change in the cutaneous manifestations during the early weeks of observation. Reexamination on July 21, 1951, revealed that the distribution and degree of hyperpigmentation remained unaltered. The number of punctate keratoses on the trunk, palms, and soles, however, was considerably reduced. Only a few widely scattered lesions were seen on the trunk, and not more than a few keratoses were present on the palms and soles. The soles were now hyperhidrotic and no longer scaly and thickened. Some maceration of the webs was evident. The palms appeared normal in texture except for a few keratoses. There was no apparent change in the nail affection.

Diagnosis: The diagnosis was arsenical pigmentation of the skin, diffuse arsenical keratoderma of the palms and soles, arsenical keratoses on the palms, soles, and trunk, and onychomycosis caused by *C. albicans*.

COMMENT

Arsenical hyperpigmentation (melanosis) was first noted (although it may very well have occurred earlier) approximately 20 months after use of Fowler's solution had been started in Case 1 and after 18 months in Case 2. The arsenical keratoses and the keratoderma of the palms and soles in Case 2 were discovered simultaneously with the hyperpigmentation. The diagnosis in both cases was based on the clinical and histological features. Increased amounts of arsenic in the urine were also demonstrated in Case 1.

Experience has shown that the time of onset for these and other cutaneous manifestations of chronic arsenicalism varies and may appear as early as one month or as late as 30 years after the ingestion or the parenteral administration of the drug.² It is mandatory, therefore, that patients be kept under careful observation and direct supervision from the time arsenotherapy is instituted (regardless of the condition under treatment) for possible signs and symptoms of intolerance. Most of the sequelae attendant on the therapeutic application of the inorganic arsenicals have, as Sulzberger and Baer³ point out, resulted from the prolonged and indiscriminate use of the drug. Properly used, with strict attention to indications and contraindications, arsenic is still a valuable therapeutic agent in the management of some diseases.

A tendency toward spontaneous regression of the keratoses and the keratoderma was noted in Case 2. It should be pointed out, however, that as a rule arsenical keratoses persist and that some give rise to squamous cell epitheliomas.⁴

SUMMARY

Two cases of cutaneous manifestations of arsenicalism following the prolonged and indiscriminate use of an arsenic containing remedy (Fowler's solution) in the treatment of bronchial asthma are described. Arsenical keratoses and keratoderma followed in one case and arsenical pigmentation in both cases.

80 Linden Blvd. (Dr. Pascher).

2. Ayres, S., Jr., and Anderson, N. P.: Cutaneous Manifestations of Arsenic Poisoning, *Arch. Dermat. & Syph.* 30: 33-43 (July) 1934.

3. Editorial Comment, in Sulzberger, M. B., and Baer, R. L.: *Year Book of Dermatology and Syphilology*, Chicago, The Year Book Publishers, Inc., 1950, pp. 191-192.

4. Montgomery, H.: Arsenic as an Etiologic Agent in Certain Types of Epithelioma: Differential Diagnosis from, and Further Studies Regarding, Superficial Epitheliomatosis and Bowen's Disease, *Arch. Dermat. & Syph.* 32: 218-236 (Aug.) 1935. MacKee, G. M., and Cipollaro, A. C.: *Cutaneous Cancer and Precancer*, New York, American Journal of Cancer, 1937, p. 23.

MULTIPLE PRIMARY MALIGNANT TUMORS OF RECTUM AND BREAST COMPLICATING PREGNANCY

REPORT OF A CASE

Emmit M. Jennings, M.D., Tucumcari, N. Mex.

The existence of malignant disease during pregnancy is fortunately a rare occurrence. Malignant tumors of the breast or rectum in the age group under 35 are also rarely reported. In an extensive review of the literature not a single case report of multiple primary tumors complicating a pregnancy was found. Because of the relatively few cases of malignancy associated with pregnancy, there is still some confusion concerning the treatment of choice in these cases. Therefore the occurrence of carcinoma of the rectum and of the breast as a complication of pregnancy and the method of treatment are worthy of being reported.

REPORT OF A CASE

Mrs. C. B., a 22-year-old Negro woman, was first seen in the Santa Rita Clinic on Jan. 31, 1949, with the chief complaint of diarrhea and bloody bowel movements. About four months previously the patient started having seven to eight watery, bloody bowel movements daily. Because of the development of weakness two weeks after onset she consulted a physician, who prescribed medication that temporarily controlled the diarrhea. The diarrhea soon recurred and lasted two to three weeks, followed by normal bowel movements for several days. No rectal examination had been done. There was no complaint of abdominal pain. Three months before, the patient had some nausea and vomiting, which lasted two months, but the patient attributed this to her pregnancy. Her last menstrual period had been three months previously, on Oct. 13, 1948.

History and Physical Examination.—The patient had had no previous pregnancies. Catamenia had begun at 14 years, occurring every 28 days with moderate flow for three days. The history by systems was noncontributory. Both parents were living and well, and there was no history of cancer in the family. The patient was a well-developed, well-nourished Negro woman. Examination of head, neck ears, nose, and throat revealed no evidence of disease. The breasts were firm, with no masses or discharge. The heart had occasional extrasystoles, with no murmurs. The blood pressure was 120/70. Examination of the abdomen revealed slight tenderness in both lower quadrants. The liver was not palpable. The pelvic examination revealed a soft cervix, with no lacerations; the adnexa were normal, the uterus was smooth and globular, located 3 to 4 cm. above the symphysis. Rectal examinations revealed a large fungating mass about 3 in. from the anal verge. The mass almost entirely encircled the rectal wall except anteriorly, and there was some fixation of the tumor mass.

Laboratory and X-Ray Findings.—A biopsy taken at this time revealed adenocarcinoma of the rectum, grade 3. The patient was immediately admitted to the hospital for surgery. An x-ray examination revealed a normal adult chest. An electrocardiogram showed sinus tachycardia and ventricular extrasystoles. Results of urinalysis were negative, except for the presence of abnormal amounts of acetone. The blood studies showed a red blood cell count of 3,840,000 per cubic millimeter, a hemoglobin value of 10.7 gm. per 100 cc., a white blood cell count of 5,000, with a normal differential count. The nonprotein nitrogen level was 24 mg. per 100 cc.

Preoperative medication consisted of two 500 cc. whole-blood transfusions, a high-carbohydrate, high-protein and low-residue diet, succinylsulfathiazole (sulfasuxadine®), 2.5 gm. five times a day, and daily enemas for five days. Two days before surgery the administration of diethylstilbestrol, 10 mg. daily, was started.

Treatment and Care.—With the patient under spinal anesthesia, a cystoscopy was done, and No. 7 ureteral catheters were inserted. No tumor infiltration was noted in the bladder. The abdomen was opened, and exploration of the abdomen revealed enlarged regional lymph nodes along the superior hemorrhoidal and inferior mesenteric vessels up to the aorta. No masses were palpated in the liver. The uterus was normal for a three and a half month pregnancy. A combined abdominoperineal resection of the rectum was done, and the colostomy was placed in the left side slightly above and lateral to the umbilicus.

The postoperative course was relatively uneventful for eight days, although the patient had an episode of mild shock immediately postoperatively. The shock was treated with stimulants and 500 cc. of whole blood. On the eighth postoperative day the patient became nauseated and vomited, and gas failed to pass through the colostomy. A Miller-Abbott tube was inserted, the distention subsided, and on the 11th day the colostomy started functioning once again. Postoperative management consisted of intravenous administration of fluids for the first three days, with a gradual increase in the diet. The patient was given antibiotics but had no temperature elevation. She also received 25 mg. of progesterone intramuscularly daily for 12 days. On the 22nd postoperative day the patient was taken to surgery for a plastic repair of the colostomy, which had become stenosed by scar tissue. This was uneventful, and the patient was discharged five days later.

The patient reentered the hospital 21 days later because of recurrence of the stenosis. She had gained 3½ lb. (1.3 kg.) in the preceding two weeks. The physical examination at this time showed no masses palpable in the breasts, and the liver was not palpable. The colostomy did not admit the little finger. Another plastic repair on the colostomy was done, and the patient was discharged three days later. She reentered the hospital on April 10, 1949, with jaundice of three days' duration. Physical examination showed a slight icteric tint in the sclera. No abnormal masses were palpated in the breasts. The uterus was enlarged to the size of a six-month gestation. A rather firm band of scar tissue was felt behind the midportion of the posterior vaginal wall.

Laboratory examinations revealed clay-colored stools that were negative for bile, an icterus index of 67, and a serum bilirubin level of 7.5 mg. per 100 cc. The urine contained bile, but no urobilinogen. The cephalin flocculation test was 1+ in 48 hours; three days later it was 3+ in 48 hours. The thymol turbidity was 6 units (0 to 5 units is normal). The stool color gradually returned to normal, as did the urine. The impression was that the patient had homologous serum jaundice.

Because excessive scar tissue developed that caused stenosis of the colostomy, it was decided to do another colostomy at the plenic flexure. A small left subcostal incision was made so as not to disturb the uterus; the splenic flexure was pulled out; and a loop colostomy done. The left lobe of the liver was palpated at this time, and a small nodule was noted. The patient was discharged on May 4, 1949.

Five weeks after discharge from the previous admission the patient was seen with the complaint of a mass in the breast noted two days previously. The mass was located in the upper inner quadrant of the left breast just medial to the nipple. It was firm, 1.5 cm. in diameter, and freely movable. The impression of several examining physicians was that the mass was a fibroadenoma.

A breast biopsy revealed a carcinoma with numerous mitotic figures. In the opinion of the pathologist the tumor was of mammary origin. In view of the patient's now gradual decline and the previously noted liver metastasis, a radical breast amputation was not done. Radiation therapy was immediately started and 24 treatments were given, totaling 2,000 r to the breast anteriorly, 1,200 r to the axilla, and 1,200 r to the supraclavicular region.

On July 20, 1949, the patient was delivered by a Norton extraperitoneal section. The infant was an apparently normal girl, weighing 5 lb. 2 oz. (3,175 gm.). Weakness developed rather rapidly following delivery, and the patient complained of severe back pain. She was discharged on July 31, 1949.

On Aug. 2, 1949, the patient was readmitted in a semicomatose condition. The previous day she had been very restless for several hours, then had mild convulsions, which occurred every

20 minutes and lasted about 1 minute. Physical examination showed the head deviated to the left, with weakness of the left arm. Numerous small nodules were noted on the skin of the abdomen. The eyes were dilated, and left nystagmus was present. A small nodule was noted in the lower outer quadrant of the right breast. The heart rate was 200 to 240, and the blood pressure was 155/100. The liver was enlarged to 6 cm. below the right costal margin and was firm and irregular. No adenopathy was noted. A serosanguinous lochia was present on pelvic examination.

A spinal puncture was done, and the initial pressure was 136 mm. of water. No blood was noted. There were 2 cells per cubic millimeter, and the protein content was 60 mg. per 100 cc. A chest roentgenogram showed no evidence of pulmonary or bony metastasis. The patient's temperature on admission was 99 F, shortly rose to 105 F and the axillary temperature varied thereafter between 100 and 105 F. Sedatives and supportive intravenous therapy were given. The convulsions were controlled, and after several days the patient seemed to be improving. Consciousness returned, and she was able to take oral nourishment. However, she again became unconscious and died on Aug. 13, 1949. Permission for an autopsy was not obtained. Clinical evidences led to the conclusion that this patient terminally had carcinoma metastatic to the liver, skin, and brain, with death resulting from brain metastasis.

COMMENT

Tumors of the visceral organs in the younger age group and multiple tumors in all ages are an infrequent occurrence. However, they do occur, and because a patient is not in the older age group, many physicians are prone to rule out malignancy without further examination. This fallacy is fortunately becoming less frequent but still occurs, as noted in the case just reported. Fowler¹ in 1926 presented an excellent review of 112 cases of malignancy in patients under 26 years of age and found 18.7% of the malignant lesions to be in the large bowel and 6.25% in the breast. Shedden,² Jordan and Chamberlin,³ and Rosenberg⁴ also stress the rarity of tumors of the bowel in persons under 35. All of these authors also stress the high mortality rate of malignancy in the younger age group. McDonald,⁵ on the other hand, feels that the younger patients have a better outlook due to their better general condition.

Multiple tumors also play a small but definite role in our discussion, because of our desire as physicians to consider all symptoms as being caused by one condition. In reviewing articles by Slaughter,⁶ Stalker, Phillips, and Pemberton,⁷ and Warren and Gates,⁸ in which they give a comprehensive review of the literature, we find an average incidence of all primary multiple tumors to be about 3.9%. Slaughter in his review of 1,868 cases found only 15 (0.8%) of the cases involving a combi-

1. Fowler, L. H.: Malignant Epithelial Neoplasms, Carcinoma, and Epithelioma Occurring in Persons Under 26 Years of Age, *Surg., Gynec. & Obst.* 43: 73-84, 1926.

2. Shedden, W. M.: Carcinoma of the Rectum and Sigmoid with Particular Reference to the Disease as Seen in Youth, *New England J. Med.* 209: 528-539, 1933.

3. Jordan, S. M., and Chamberlin, D. T.: Cancer of the Digestive Tract in the Young, *S. Clin. North America* 17: 815-820, 1937.

4. Rosenberg, H.: Carcinom im jugendlichen, *Ztschr. Krebsforsch.* 41: 230-238, 1934.

5. McDonald, I.: Mammary Carcinoma: A Review of 2,636 Cases, *Surg., Gynec. & Obst.* 74: 75-82, 1942.

6. Slaughter, D. P.: The Multiplicity of Origin of Malignant Tumors: A Collective Review, *Internat. Abstr. Surg.* 79: 89-98, 1944.

7. Stalker, L. K.; Phillips, R. B., and Pemberton, J. De J.: Multiple Primary Malignant Lesions, *Surg., Gynec. & Obst.* 68: 595-602, 1939.

8. Warren, S., and Gates, O.: Multiple Primary Tumors: Survey of the Literature and a Statistical Study, *Am. J. Cancer* 16: 1358-1414, 1932.

nation of carcinoma of the breast and large bowel. In Warren and Gates' study, the youngest patient reported with the combination of breast and gastrointestinal malignancy was 42 years of age. The average age reported by all writers is 59 to 61.

In reviewing the literature on carcinoma of the rectum or large bowel complicating pregnancy Banner, Hunt, and Dixon⁹ in 1945 reported all known cases to date and added 7 more cases to the 62 they had compiled from the literature. Subsequently, Finn and Lord,¹⁰ Putzki and his colleagues,¹¹ Swartley and co-workers,¹² and Sadugor¹³ have added one case and Bacon and Rowe¹⁴ four cases. Thus a total of 77 cases of carcinoma of the large bowel complicating pregnancy have been found in the literature up to the present.

With such a paucity of material available to review and considering that only a small percentage of these cases have occurred since the advent of improved surgical technique and endocrine and antibiotic therapy, there is still confusion regarding the proper management. Standard textbooks in obstetrics, such as Stander,¹⁵ give us very little help on the subject. Russell¹⁶ recommended that if the tumor is found early in pregnancy, labor should be induced and a radical operation done later. In advanced pregnancy with a viable fetus a cesarean section, hysterectomy, and detachment of the rectum should be performed, so a Rehn or Liermann procedure can be done later. Tchegotarevsky (1908) recommends removal of operable tumors as soon as possible, termination of the pregnancy before operation unless it is early and there is a possibility of preserving the pregnancy even with radical operation, or a colostomy, if the tumor is inoperable.

Berkeley, Bonney, and MacLeod¹⁸ advocate that in acute obstruction, regardless of the length of pregnancy, a hysterectomy, colostomy, and later a resection be done. If the tumor is operable and the rectum is not obstructed, the uterus should be emptied, removed, a colostomy

performed, and later a resection, or a hysterectomy and colostomy done in early months. In later months of the pregnancy conservative methods may be used, then a cesarean section and colostomy should be performed. Adair¹⁹ favors immediate interruption of the pregnancy as soon as possible after the diagnosis is made, if there is any possibility of a cure, and resection of the colon as soon as possible. I agree in part with Bacon and Rowe, who recommend in early pregnancy removal of the tumor with relative disregard to the pregnancy. However, in the second trimester they recommend a Porro section and resection of the lesion if the patient's condition warrants it. In the third trimester they recommend a cesarean section and hysterectomy. If the condition of the patient permits, the resection is also done at the time, otherwise the resection is made in two to four weeks after delivery.

In the more recent papers there is a growing tendency to treat the carcinoma independently of the pregnancy. Bacon, quoting Maud Slye, states that extragenital cancer (except in the breast) is not influenced by pregnancy, and, therefore, if this is true there is absolutely no indication for hysterectomy or abortion. Slye²⁰ found in mice that in general there is a retardation of tumor growth during pregnancy, since the body feeds the fetus rather than the tumor. Kross²¹ similarly reports that growth of mammary and uterine cancers is hastened, but there is no effect or actual slowing of extragenital cancer. Bainbridge, on the other hand, feels that pregnancy speeds up all cancer growth.

With these facts in mind I feel that the treatment of choice in carcinoma of the large bowel complicating pregnancy is to treat the disease regardless of the pregnancy. True, the enlargement of the uterus during the second trimester offers some technical difficulties, but they are not insurmountable. However, should the uterus be involved in an extension of the malignant lesion, then if the lesion is to be removed the uterus must be included in the resection. Once again, though, this follows the dictum of treating the malignant lesion regardless of the pregnancy. Although each case must be treated individually in my opinion the following treatment should be recommended in carcinoma of the rectum or sigmoid during pregnancy. 1. In the first and second trimesters, the lesions should be resected either by abdominoperineal resection or by end-to-end anastomosis. 2. In the third trimester, cesarean section should be performed in the seventh and eighth months, and, depending on the status of the patient, resection of the malignant lesion should be made at this time or after two to four weeks. This may be the time to do a preliminary colostomy. In the ninth month labor may be induced with delivery from below if the lesion is not too large, followed in two to four weeks by resection, or the criteria set down for the seventh and eighth months may be used. Antibiotics and endocrine preparations should be a definite part of the preoperative and postoperative regimen.

At no time should it be necessary to attack the life of fetus directly. However, as previously stated, if the uterus is involved by direct extension of the tumor, it should be removed. If the resection is done post partum,

9. Banner, E. A.; Hunt, A. B., and Dixon, C. F.: *Pregnancy Associated with Carcinoma of the Large Intestine*, Surg., Gynec. & Obst. **80**: 211-216, 1945.

10. Finn, W. F., and Lord, J. W.: *Carcinoma Producing Acute Intestinal Obstruction During Pregnancy*, Surg., Gynec. & Obst. **80**: 545-548, 1945.

11. Putzki, P. S.; Scully, J. H.; Kotz, H.; Kaufman, and Torrey: *Carcinoma of the Colon Producing Acute Intestinal Obstruction During Pregnancy*, Am. J. Surg. **77**: 749-754, 1949.

12. Swartley, W. B.; Newton, Z. B.; Hartman, J. C., and Stayman, J. W., Jr.: *Perforated Carcinoma of the Large Intestine Complicating Pregnancy: Successful Operative Management*, Ann. Surg. **125**: 251-256, 1947.

13. Sadugor, M. G.: *Carcinoma of the Rectum Complicating Pregnancy*, California Med. **70**: 489-490, 1949.

14. Bacon, H. E., and Rowe, R. J.: *Abdominoperineal Proctosigmoidectomy for Rectal Cancer Complicating Pregnancy: Report of 4 Cases*, South. M. J. **40**: 471-479, 1947.

15. Stander, H. J.: *Williams Obstetrics: A Textbook for the Use of Students and Practitioners*, New York, Appleton-Century-Crofts Company, 1941, p. 1197.

16. Russell, A. W.: *Cancer of the Rectum as a Complication of Pregnancy and Labour*, Scottish M. & S. J. **12**: 409-507, 1903.

17. Deleted on proof.

18. Berkeley, C.; Bonney, V., and MacLeod, D.: *The Abnormal in Obstetrics*, London, William Wood & Company, 1938, p. 120.

19. Adair, F. L.: *Obstetrics and Gynecology*, vol. 1 and 2, Philadelphia, Lea & Febiger, 1940, p. 623.

20. Slye, M.: *The Relation of Pregnancy and Reproduction to Tumor Growth; Incidence and Inheritability of Spontaneous Tumors in Mice*, J. Cancer Res. **5**: 25, 1920.

21. Kross, I.: *Pregnancy and Tumor Growth*, J. Cancer Res. **6**: 245-250, 1921.

22. Deleted on proof.

a hysterectomy need not be done. If an abdominoperineal resection is done early in the pregnancy, the delivery of choice should be from below, unless there is some contra-indication on pelvic examination, such as developed in the case reported.

As can be noted from review of the literature, carcinoma of the breast during pregnancy is seen far more frequently than carcinoma of the rectum. Lee²³ in reviewing 1,827 cases of carcinoma of the breast reported 306 cases occurring in women under 40 years of age. Of the 306 women, 11 were pregnant and 14 lactating. Harrington²⁴ reports that 2% of all his radical mastectomies were on women who were pregnant or lactating. Brooks and Proffitt²⁵ conclude that there is no evidence to support the idea that carcinoma of the breast is originated by pregnancy. They do feel, however, that the rate of growth of carcinoma of the breast is increased by pregnancy. Kilgore²⁶ reported 49 cases of cancer during pregnancy, with 70% cure by radical mastectomy if the axillary nodes were not involved and 11.5% cure if axillary nodes were involved.

The argument regarding the treatment of carcinoma of the breast during pregnancy continues to be a question. If we are to agree with Haagensen and Stout²⁷ or Lenz²⁸ the mortality from cancer will certainly be high. Still others, Tyler²⁹ and Geschickter,³⁰ recommend abortion followed by radical mastectomy, unless the procedure is done late in pregnancy, when delivery should first be attempted, then the radical mastectomy done.

A third thought, as followed by Harrington,³¹ Cole and Rossiter,³² Power,³³ and Smith,³⁴ is that the patient should have a radical mastectomy and the pregnancy should be allowed to go to term. Certainly the figures of Harrington (see table) and Kilgore give a sound basis for this program. These results alone indicate that, although the results are not as good as on nonpregnant patients, there is a definite survival rate following mastectomy and we should avail the patient of this by using a radical procedure, with the same criteria for operability as if the patient were not pregnant.

Smith³⁴ in a review of the effect of pregnancy on malignant tumors states that those patients whose pregnancies were not interrupted did as well or better than those whose pregnancies were interrupted when first seen. Taylor³⁵ and de Cholnoky³⁶ in the study of breast carcinoma in youth feel that carcinoma in the young tends to be of higher grade malignancy and metastasize earlier. Taylor notes that in carcinoma of the breast of equivalent extent and equal grade of malignancy the age of the patient alone does not affect the outlook, the five-year survival rates being about equal.

Considering Harrington and Smith's figures the most promising in the final analysis for both mother and infant, I feel that treatment should consist of radical mastectomy as soon as possible. This should be done regardless of the stage of the pregnancy. The operation should be followed by x-ray therapy. The decision to do a radical mastectomy, however, should depend, not on the pregnancy, but on whether the patient would have a radical mastectomy if she were not pregnant. It is not within the realm of this paper to include a complete discussion of treatment of radical mastectomies postoperatively.

COMMENT

Unfortunately, one case, especially one terminating fatally, is a poor basis on which to draw many conclusions. However, in the case reported there are several points in the treatment that we would like to stress. 1. A thorough physical examination was made. The malignant lesion in this patient's rectum was noted the first time the patient had a rectal examination. Had the first physician examined this patient thoroughly her ultimate prognosis might have been much better. In Bacon's review he noted that 64 of the 70 lesions of the rectum were palpable. 2. Similarly, we must be ever alert to developments in the course of the disease. The breast lesion was noted only eight to nine weeks after the patient had been in the hospital and had had a complete physical examination. 3. As soon as possible after discovery of the malignant lesion this patient had an abdominoperineal resection. Unfortunately, with regional lymph nodes already involved as far down as the aorta, her prognosis, pregnant or not, was poor. 4. The original desire to allow this patient to deliver from below was abandoned because of excessive scar tissue bands, which could be pal-

*Survival Rates Following Radical Mastectomy in Pregnant or Lactating Patients**

Yr. After Operation	Patients With Metastasis		Patients Without Metastasis	
	No. Patients Traceable	% Survivals	No. Patients Traceable	% Survivals
3	84	15.5	15	60
5	78	7.7	14	57.1
10	64	3.1	13	38.5
15	48	2.1	9	22.2
20	27	0	5	20

* Data based on a table by Harrington.²⁴

pated deep in the posterior vagina. Extraperitoneal section was done because the colostomy caused a contaminated abdominal wall. 5. Although radical mastectomy would have been the procedure of choice, biopsy only was done because of the previously noted liver metastasis. A desire to retard the lesion was the reason

23. Lee, B. J.: Significant Problems for the Obstetrician in the Field of Mammary Cancer, *Am. J. Obst. & Gynec.* **20**: 775-781, 1930

24. Harrington, S. W.: Results of Radical Mastectomy in 5,026 Cases of Carcinoma of the Breast: Various Clinical and Pathologic Factors Which Influence Prognosis, *Pennsylvania M. J.* **43**: 413-427, 1940.

25. Brooks, B., and Proffitt, J. N.: Influence of Pregnancy on Cancer of the Breast, *Surgery* **25**: 1-11, 1949.

26. Kilgore, A. R.: Tumors and Tumor-Like Lesions of the Breast in Association with Pregnancy and Lactation, *Arch. Surg.* **18**: 2086-2098, 1929.

27. Haagensen, C. D., and Stout, A. P.: Carcinoma of the Breast: Criteria of Operability, *Ann. Surg.* **118**: 859-870, 1943.

28. Lenz, M.: Tumor Dosage and Results in Roentgen Therapy of Cancer of the Breast, *Am. J. Roentgenol.* **58**: 67-74, 1946.

29. Tyler, G. T.: What Advice Shall We Give Regarding Pregnancy in Patients with Mammary Cancer? *Virginia M. Monthly* **47**: 375, 1920.

30. Geschickter, C. F.: Diseases of the Breast: Diagnosis, Pathology, Treatment, ed. 2, Philadelphia, J. B. Lippincott Co., 1945, p. 175.

31. Harrington, S. W.: Carcinoma of the Breast: Results of Surgical Treatment When the Carcinoma Occurred in the Course of Pregnancy or Lactation and When Pregnancy Occurred Subsequent to Operation, 1910-1933, *Ann. Surg.* **106**: 690-700, 1937.

32. Cole, and Rossiter.: The Breast, in Lewis, D.: Practice of Surgery, Clinical, Diagnostic, Operative, Postoperative, vol. 5, Hagerstown, Md., W. F. Prior Co., 1930, Chap. 6, p. 85.

33. Power, H. A.: Pregnancy Complicating Carcinoma of the Breast, *Pennsylvania M. J.* **45**: 1049-1050, 1942.

34. Smith, F. R.: Effect of Pregnancy on Malignant Tumors, *Am. J. Obst. & Gynec.* **34**: 616-633, 1937.

35. Taylor, G. W.: Carcinoma of the Breast in Young Women, *New England J. Med.* **215**: 1276-1278, 1936.

36. de Cholnoky, T.: Mammary Cancer in Youth, *Surg., Gynec. & Obst.* **77**: 55-60, 1943.

for x-ray therapy. Some might argue that irradiation in this case was a useless procedure. This fact was considered but it was felt that the patient should have the benefits of any doubt.

SUMMARY AND CONCLUSIONS

This is as far as I know the first case reported of multiple primary tumors complicating the same pregnancy. A case report of a 22-year-old Negro woman with carcinoma of the rectum and carcinoma of breast, both discovered and treated during the pregnancy, is given.

The literature is reviewed and tumors of the younger age groups as well as multiple tumors are noted to be rare.

Carcinoma of the rectum during pregnancy is discussed. The literature contained reports of 77 cases, with one added here for a total of 78. In carcinoma of the rectum I recommend the following measures: (1) in the first and second trimesters a resection of the lesion either by abdominoperineal resection or section with an end-to-end anastomosis; (2) in the seventh and eighth months a cesarean section and, depending on the status of the patient, a resection of the malignancy at this time or after two to four weeks; and (3) in the ninth month induction of labor, with delivery from below followed in two to four weeks by resection, or the procedure recommended for the seventh and eighth months. The uterus is to be removed only if involved by direct extension of the tumor. Delivery from below is to be allowed only if rectal and pelvic findings permit.

Carcinoma of the breast during pregnancy is discussed, and the treatment recommended is radical mastectomy followed by x-ray therapy, regardless of the stage of pregnancy. However, if the patient is due within one to two weeks, it might be preferable to perform delivery first. The criteria for operability should be the same as for nonpregnant patients. Treatment of carcinoma during pregnancy is reviewed with the conclusion that the malignant disease should be eradicated and the pregnancy allowed to continue. I would like once again to place special emphasis on the fetus. Too many physicians are prone to consider abortion a panacea for all malignant disease complicating pregnancy. However, the excellent review of Smith³¹ on the effect of pregnancy on malignant tumors would be enlightening to many physicians.

Box 321.

Pregnancy After Forty.—From his very conception the infant born of parents past 40 has an environment different from that which he might have had 20 years earlier. At this late date in the human reproductive period, the fetus is more apt to share his uterine covering with fibromyomata. His attitude in utero is more inclined to be influenced by such a condition as a relaxed abdominal wall, and his mother has had a greater opportunity to develop thyroid disease, changes in her cardiovascular system, or even cancer. Embryonic and fetal development may be influenced directly by local pelvic pathology or indirectly by conditions of a systemic nature. During the two decades in which he might have been born the infant's parents have had a greater span of emotional experience; their earning powers have been reduced, and in fact, the entire world into which the new baby is born is different. In many respects, the infant has postmature characteristics.—John Parks, M.D., *Pregnancy After Forty, Geriatrics*, December, 1951.

REITER'S DISEASE

REPORT OF A CASE IN A WOMAN

Solomon Rinkoff, M.D., New York

In 1916 Reiter¹ described a clinical entity in a German lieutenant characterized by abdominal cramps and bloody diarrhea, followed by urethritis, conjunctivitis, and later by arthritis of the left knee, right elbow, left wrist, and joints of the fingers of the right hand in that order. Subsequently cystitis, edema of the prepuce, iritis, splenomegaly, and pustular lesions of the hip also developed in this patient. Reiter was unable to influence the course of the disease by any therapy at his command, but recognized that the symptoms did not result from either gonorrhea or dysentery. About the same time Fiessinger and Leroy² in France and Macfie³ in Africa made independent reports of this disease.

Many reports of this syndrome followed in the French, German, and Scandinavian literature, but it was not until 1942 that the disease was recognized in America and reported by Bauer and Engleman.⁴ Since then there have been numerous reports in the American literature,⁵ but except for one questionable case⁶ they have all been in men. For this reason I wish to report the occurrence of this disease in a woman.

REPORT OF A CASE

C. L., a 49-year-old married white woman, was referred to me by Dr. H. L. Greene on May 28, 1948, and was admitted the same day to the Bronx Hospital. Frequency and burning on urination had developed about three weeks prior to admission. Her urine contained numerous pus clumps. She was given methenamine mandelate (mandelamine®) tablets, but diarrhea developed and the drug was discontinued. She was then given phenylazodiaminopyridine (pyridium®) hydrochloride tablets without relief of symptoms. Five days prior to admission she had received two injections of procaine penicillin G totaling 600,000 units. Four days prior to admission conjunctivitis developed and the next day pain and swelling in the right wrist and stiffness of the fingers of the right hand appeared. Low-grade fever developed about a week prior to admission.

Physical examination revealed an acutely ill white woman, with a temperature of 101.6 F. Both eyelids were red and swollen, with encrusted margins. There were marked congestion of the conjunctivas and free pus in the conjunctival sacs. Photophobia was present. The throat was normal. The heart rhythm was regular, with no murmurs; blood pressure was 120/80. The lungs and abdomen were normal. Vaginal examination revealed a profuse discharge. There was marked redness, swelling and limitation of motion of the right wrist. The fingers of the right hand were also stiff. A diagnosis of Reiter's disease was made.

1. Reiter, H.: Ueber eine bisher unerkannte Spirochäteninfektion (Spirochaetosis arthritica), *Deutsche med. Wchnschr.* **41**: 1535, 1916.

2. Fiessinger, N., and Leroy, E.: Contribution à l'étude d'une épidémie de dysenterie dans la Somme, *Bull. et mém. Soc. méd. hôp. Paris* **40**: 2030, 1916.

3. Macfie, J. W. S.: Urethral Spirochaetosis, *Parasitology* **9**: 274, 1917.

4. Bauer, W., and Engleman, E. P.: Syndrome of Unknown Etiology Characterized by Urethritis, Conjunctivitis, and Arthritis (So-Called Reiter's Disease), *Tr. A. Am. Physicians* **57**: 307, 1942.

5. (a) Colby, F. H.: Renal Complications of Reiter's Disease, *J. Urol.* **52**: 415, 1944. (b) Rosenblum, H. H.: So-Called Reiter's Disease: Triad of Acute Arthritis, Conjunctivitis and Urethritis, *U. S. Nav. M. Bull.* **44**: 375, 1945. (c) Hollander, J. L.; Fogarty, C. W., Jr.; Abrams, N. R., and Kydd, D. M.: Arthritis Resembling Reiter's Syndrome: Observations on 25 Cases, *J. A. M. A.* **129**: 593 (Oct. 27) 1945.

6. Lever, W. F., and Crawford, G. M.: Keratosis Blennorrhagica Without Gonorrhea (Reiter's Disease), *Arch. Dermat. & Syph.* **49**: 389 (June) 1944.

Immediately after admission smears and cultures were taken from the eyes and cervix. A specimen of urine obtained by catheterization was also examined and cultured. All smears and cultures were negative for *Neisseria gonorrhea*. The urine contained numerous clumps and pus cells, but no bacteria. The vaginal smear revealed numerous pus cells and gram-positive cocci and rods. Pus cells but no bacteria were seen on the smear taken from the eyes. Salicylate therapy, 90 grains (6 gm.) daily, with meperidine (demerol[®]) hydrochloride for pain was begun.

On May 29 the patient was examined by Dr. Herman Ballen of the ophthalmological service, who made the following observations: Both lids were red and swollen, with encrusted margins. In the conjunctivas the vessels were dilated and congested, with free pus in the conjunctival sacs. The right pupil was larger than the left. The left pupil was irregular and reacted sluggishly to light. There were posterior adhesions. The right pupil was round and reacted to light. On dilation with 1% solution of homatropine hydrochloride, the margin of the left pupil adhered to the capsule. The anterior capsule of the left eye, over the area of the pupil, was covered with organized exudate. The aqueous humor of the left eye was cloudy. Reexamination on June 1 by Dr. Ballen revealed that the globe of the right eye was soft and white. The pupil was dilated, and the anterior chamber was clear. The fundus was normal. There were marked ciliary injections in the left eye; the globe was tender to touch. The pupil was dilated and adherent posteriorly; the aqueous humor was cloudy. There was an old, organized exudate on the anterior capsule in the pupillary area, with new exudate on the anterior capsule. The fundus could not be visualized because of the inflammatory reaction in the anterior chamber and anterior capsule. The intraocular tension in the right eye was 20 mm. (Schoetz). The clinical impression was iridocyclitis of the left eye. The diagnosis was acute conjunctivitis of unknown origin, with iritis of the left eye (Reiter's disease).

The treatment he prescribed consisted of the application of a 2% solution of homatropine hydrochloride every 4 hours for 24 hours. If the intraocular pressure remained normal, this was to be changed to a 1% solution of atropine sulfate three times daily. A solution of benzalkonium (zephiran[®]) chloride 1:4,000 was to be administered every two hours. Hot compresses were to be applied for 10 minutes every two hours.

About June 3 the patient developed arthritic pain in cervical vertebrae and the right knee. The pain and swelling of the right wrist persisted. On June 4 she was unable to turn her head because of cervical pain and immobility. On June 9 the right eye was almost normal. However, the left eye still had ciliary injection and exudate over the anterior capsule; the fundus could not be visualized well. She also had a good deal of pain in the left eye. On this day the right temporomandibular joint became tender on palpation and motion.

On June 11 the left eye appeared improved. The patient could count fingers at 3 ft. The intraocular tension was normal. Ciliary injection and exudate in the anterior capsule were diminishing, and the fundus could be seen, but not clearly. The patient still had joint pains, but they were not severe and were controlled by salicylates.

The patient had an exacerbation of the conjunctivitis of the right eye on June 16, but this subsided in a few days. Her general condition improved. The conjunctivitis and iritis of the left eye gradually cleared and visual acuity increased. The arthritic manifestations also diminished in intensity and frequency. During hospitalization her temperature varied as follows: 100 to 101.6 F, first week; 100 to 102 F, second week; 100 to 101 F, third week; 99.6 to 100.6 F, fourth week; and 100 F in the evening of the week of discharge. The urine cleared so that there was only an occasional pus cell, and she was discharged for further care by her family doctor on June 26, 1948.

Laboratory Data.—On the day of admission the urine had a specific gravity of 1.016 and 1+ albuminuria, but contained no sugar. Numerous pus clumps were seen on microscopic examination. On June 17 there were 50 to 100 white blood cells per low power field and an occasional clump. On that day urine culture revealed a gram-negative rod of the paracolon group. The hemoglobin value was 11 gm. (76%), and there were 3,680,000 red blood cells and 6,750 white blood cells, with 49% polymorphonuclear leukocytes, 15% basophil cells, 28% lymphocytes, and 7% monocytes. The erythrocyte sedimentation

rate was 42 mm. per hour. Electrocardiography revealed no evidence of rheumatic activity or myocardial disease. Intravenous urography revealed no abnormalities of the kidneys.

I saw the patient on Dec. 4, 1949, and Jan. 12, 1950. She still had arthralgia of the cervical spine and some stiffness of the finger joints of the right hand. An electrocardiogram revealed no cardiac pathology and x-ray examination of the cervical spine and hands revealed no arthritic changes. The erythrocyte sedimentation rate and blood cell count were normal. There was no conjunctivitis, and the urine contained no pus, albumin, or sugar.

COMMENT

Etiology and Epidemiology.—No definite cause for this disease has been determined. Reiter¹ found atypical spirochetes in the blood, and Macfie² found them in the urethral discharge. Some investigators found high agglutination titers against dysentery organisms and therefore thought that these might be the cause of the disease. However, no dysentery organisms were found in the blood, stool, urethral, or conjunctival secretions. Others found anhemolytic streptococci or enterococci in the blood cultures in some cases. Dienes⁷ cultured pleuropneumonia-like organisms from the urethra of a man with urethritis and arthritis. These so-called L-organisms have also been cultured from the vaginas of women with leukorrhea. Beveridge⁸ isolated these L-organisms from the urethras of men who had nonspecific urethritis. He believes that this L-organism is normally a saprophytic inhabitant of the female genital tract and that after transfer through sexual contact, it might, under certain conditions of virulence and dosage, cause a pathologic condition in the male. Harkness⁹ supports the L-organism hypothesis and states that he has found inclusion bodies in the urethral and conjunctival smears in every one of five cases of Reiter's disease seen by him in a five-year period.

The organism is extremely pleomorphic, changes its shape, and may reproduce by sexual and asexual means. In one form it may be filtered like a virus, and in another it may lead an intracellular parasitic existence. The descriptions and drawings of the organisms found by Reiter and Macfie resemble this pleuropneumonia-like organism. The mode of entry of this organism also is not clear. In cases in which diarrhea is present, entrance through the intestinal tract is likely, the agent then causing damage either to the intestinal wall or to the mucosa. In cases without diarrhea the agent probably enters through the genital tract.

Reiter's disease has been reported from Europe, Africa, the Pacific Islands, and the United States. While almost entirely limited to men in the third and fourth decades, it may occur in women.

Pathology.—Biopsies of the knee joints were obtained by Bauer and Engleman,⁴ Wepler,¹⁰ and Hollander and his co-workers.^{5c} These revealed congested and purplish synovia. Microscopic examinations revealed intense inflammatory reactions limited to the superficial synovial layers, and not involving the supporting collagen, fibrous

7. Dienes, L., and Smith, W. E.: Relationship of Pleuropneumonia-Like (L) Organisms to Infections of Human Genital Tract, *Proc. Soc. Exper. Biol. & Med.* 50: 99, 1942.

8. Beveridge, W. I. B.: Isolation of Pleuropneumonia-Like (L) Organisms from Male Urethra, *M. J. Australia* 2: 479, 1943.

9. Harkness, A. H.: Cutaneous Manifestations of Gonorrhoea, *Brit. J. Ven. Dis.* 21: 93, 1946.

10. Wepler, W.: Zur Morphologie und Pathogenese der post-dysenterischen Polyarthritis, *Beitr. path. Anat.* 106: 289, 1942.

connective tissues, or vessel walls. The synovia were thrown into large club-like projections in which the abundant capillaries were all dilated. Each projection was distended by a heavy lymphocytic infiltrate mixed with a few plasma cells and a few neutrophils. No fibrinous exudate was found. The intima was approximately 6 to 10 layers deep. Only a few perivascular collections of lymphocytes and plasma cells could be found. There were no well-defined new capillaries, and the intense hyperemia consisted of dilation of preexisting capillaries.

Symptoms and Course.—Diarrhea often precedes by 10 to 30 days the development of the triad of urethritis, conjunctivitis, and arthritis. In fact, the French clinicians hesitate to make the diagnosis unless diarrhea was present. However, the diarrhea is often mild, and unless specifically questioned about diarrhea, the patient may forget to mention it. It is possible that the diarrhea our patient had was not due to the methenamine mandelate she received.

From 10 to 30 days after the enteric phase, conjunctivitis and urethritis appear, one or the other preceding by a day or two. The conjunctivas become hyperemic and edematous, and yellowish mucopurulent discharge appears. Most commonly only conjunctivitis results, but occasionally keratitis, iritis, and iridocyclitis occur. With the onset of urethritis the patient complains of dysuria and frequency, and the urethra discharges a yellow mucopurulent substance. Not infrequently cystitis, prostatitis,⁴ and prostatic abscess^{5a} have been noted. Colby^{5a} described pyelonephritis as a complication. The urethritis and conjunctivitis last throughout the entire course of the disease, with occasional remissions and exacerbations.

As the disease progresses, the weight-bearing joints, particularly the knees and ankle, become involved. Less frequently, the hips, shoulders, wrists, finger joints, and even the vertebrae may be affected. The involvement is usually multiple and the arthritis is migratory, as in acute rheumatic fever. Tendovaginitis has been described. The roentgen examination of the joints does not reveal destructive changes. Osteoporosis may develop after four to six weeks. Ankylosis occurs rarely. Hydrarthroses are common, and serous fluid containing equal proportions of polymorphonuclear leukocytes and lymphocytes may be obtained on tapping. Cultures of the joint fluid are usually sterile. During this period the patient has a low-grade fever. There is no anemia as a rule, but there is leukocytosis and the erythrocyte sedimentation rate is increased.

Adenopathy is found frequently, and splenomegaly has been described occasionally. Pleuritis has also been mentioned. In a small proportion of cases, late in the disease, skin lesions appear. They begin as small superficial vesicles, change into small ulcers, and finally heal, leaving hyperkeratotic scars—the so-called keratosis blenorragica of nongonorrheal origin. There is a predilection for these lesions over the affected joints, especially in the lower extremities, and over the scrotum and penis. Incomplete syndromes have also been reported. Urethritis and arthritis without conjunctivitis have been reported by Hollander and his colleagues.^{5c}

The prognosis for life is excellent. Occasionally extensive ocular injuries occur, and ankylosis may also

develop. The disease usually lasts from two to four months. However, relapses are not unusual and may occur over a period of many years. Many types of therapy have been tried, including sulfonamides, penicillin, arsenicals, gold, and fever therapy, all without effect.

SUMMARY

A case of Reiter's disease in a woman that illustrates different features of the disease is described. The earliest symptom is usually diarrhea, followed by urethritis, conjunctivitis, and migratory arthritis. The disease has been reported from Western Europe, America, and the Pacific Islands. The cause of the disease is still obscure, the most likely etiologic agent being a pleuropneumonia-like organism. The portal of entry is either the gastrointestinal or the urethral tract. The prognosis for life is good; permanent ocular and joint lesions, though unusual, may occur.

1749 Grand Concourse.

MEDIAL APPROACH FOR PARAVERTEBRAL SOMATIC NERVE BLOCK

Wallace M. Shaw, M.D., Hollis, N. Y.

The purpose of this paper is to describe a paravertebral approach that provides accurate localization of the needle in relation to the nerve for anesthetic blocking of the thoracic and lumbar spinal nerves. The technique can be termed the medial route for paravertebral somatic nerve blocking. It depends on contacting the lamina of the vertebra at the level of the intervertebral foramen and then redirecting the needle laterally and anteriorly to approach the intercostal or lumbar nerve.

The principal techniques in use at present depend on utilization of a rib or transverse process as the major landmark. In one technique¹ the rib (or in the lumbar region, the transverse process) below the nerve is contacted 4 cm. from the midline and the needle is then redirected cephalad, medially, and anteriorly to parallel the course of the spinal nerve. If the needle deviates even slightly from the proper direction, the anesthetic solution may be deposited outside the fascial plane in which the nerve is located. With better technique the needle may traverse the intervertebral foramen and enter the subarachnoid space. The more accurate the technique the greater the likelihood of subarachnoid injection, either through the intervertebral foramen or the dural sleeve prolonged around the nerve. If the needle enters the dural prolongation, aspiration of spinal fluid may be impossible, and this usual warning is then absent.

In another commonly used technique² the rib or transverse process above the nerve to be blocked is contacted, and the needle is redirected caudad, medially, and anteriorly to cross the spinal nerve. This technique reduces the possibility of intraspinal injection, but also decreases the accuracy of the localization and often a large amount of solution must be infiltrated to produce anesthesia.

From the Department of Anesthesia, Prospect Heights Hospital, Brooklyn.

1. Rovenstine, E. A.: Personal communication to the author.

2. Labat, G.: *Regional Anesthesia: Its Technic and Clinical Application*, ed. 2, Philadelphia, W. B. Saunders Company, 1928.

TECHNIQUE OF THE MEDIAL APPROACH

Localization.—The paravertebral block is most easily performed with the patient prone and a small soft pillow placed beneath the chest so that the scapulas fall forward for thoracic blocks. The operator stands on the side opposite the one to be blocked. The procedure may also be performed with the patient in the lateral recumbent or sitting position.

The anatomical level of the segmental nerve to be blocked is determined. The important area to be localized is the space between the transverse processes, the location of both the intervertebral foramen and the spinal nerve. The intercostal space, if palpable, is followed backward as far as possible and projected medially to a point 1 cm. from the midline. This point overlies the lamina at the level of the intervertebral foramen. If the intercostal space cannot be felt, the vertebral spines are used as a guide. The 1st, 2nd, 3rd, and 12th thoracic nerves are approximately opposite the corresponding vertebral spines. The other thoracic nerves are approximately opposite the spine of the next higher vertebra. In the lumbar area the intervertebral foramina are level with the interspinous spaces.

Placement.—At the level of the intervertebral foramen as determined above a skin wheal is raised with anesthetic solution 1 cm. from the midline on the side to be blocked. A 3 in. (7.6 cm.) 22-gage needle is inserted at right angles to the frontal plane until the lamina of the vertebra is contacted (see the accompanying figure). The needle is partially withdrawn, and its point is redirected more laterally until it just slips off the edge of the lamina. The needle is then advanced 1 cm. further. If the needle still contacts bone at an angle of about 45 degrees, it is probably "walking" along a transverse process or rib. In this event the needle is directed either superiorly or inferiorly through the same skin wheal or a new one, and again is probed more and more laterally until bone is no longer contacted. The needle is then advanced 1 cm.

The point of the needle then lies in a triangular space bounded medially by the body of the vertebra, anteriorly by the pleura or peritoneum, and dorsally by the fascial covering of the sacrospinalis muscle. This space contains loose areolar and fatty tissue and the rami communicantes; it is traversed by the spinal nerve and blood vessels. Anesthetic solutions injected into this space are close to the spinal nerve and diffuse readily to produce anesthesia.

Precautions.—When the needle has been correctly placed, a careful check should be made of whether the subarachnoid space, pleural cavity, or a blood vessel has been entered, as should be done during paravertebral injections by any route. If spinal fluid or blood is aspirated through the needle, the needle should be withdrawn and the space reentered after about five minutes. If air is aspirated, indicating puncture of the lung, the procedure should be discontinued and the patient carefully watched for development of pneumothorax.

Injection.—If no spinal fluid, blood, or air is aspirated, 4 to 7 cc. of anesthetic solution is injected. If more than one nerve must be anesthetized, the first needle should be left temporarily in place to guide placement of the remaining needles.

ADVANTAGES OF THE MEDIAL APPROACH

Although it might appear great at first glance, the risk of pneumothorax is really slight with this technique. Exploratory probing is done while the needle is superficial to the vertebral lamina and transverse process, and the needle is not manipulated once contact with bone has been lost. For these reasons the danger of puncturing the pleura is less than with other methods in which the needle is manipulated in soft tissue 3 to 6 cm. from the nearest bony landmark, and the needle traverses a narrow channel bordered by the pleura anteriorly and the intervertebral foramen medially. Even a small anterior deviation can result in perforation of the pleura and lung.

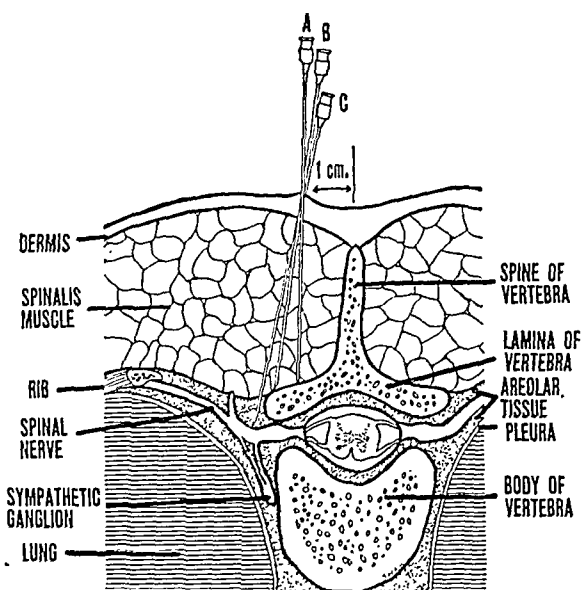
Intraspinal injection is almost impossible by the medial approach, because the needle is directed laterally, away from the intervertebral foramen. However, conceivably a

long dural sleeve around the nerve might be pierced. Although this possibility is remote, it must be carefully avoided.

The ease with which spinal nerves may be successfully blocked is a distinct advantage of the medial approach. Superficial and deep bony landmarks are easily identified and accurate placement of the needle is not difficult. Paresthesias along the distribution of the nerve are frequently elicited, indicating proximity to the nerve.

RESULTS

The medial route has been used in seven patients to anesthetize 33 nerves, with failure to block only two that were reinjected successfully. Effective anesthesia has been possible with as little as 2 cc. of anesthetic solution, denoting accurate placement. The anesthetic agents employed include 2% procaine hydrochloride solution, 0.2% tetracaine (pontocaine®) hydrochloride solution, 5% beta-diethylaminoethyl-para-ethoxybenzoate (intra-



Diagrammatic cross section through a thoracic vertebra, showing positions of the needle in blocking the spinal nerve by the medial route. A, needle in contact with the lamina. B, needle sliding laterally along lamina. C, needle in correct position for injection.

caine®) in oil, 0.1% isoamylhydrocupreine (eucupin®) dihydrochloride plus 3% ethylaminobenzoate ("benzocaine") in oil, and absolute alcohol. There were no instances of pneumothorax, intraspinal puncture, post injection neuritis, or any other complication attributable to the nerve blocking procedure. Entrance of a needle into a blood vessel was easily recognized on two occasions, and in each instance the nerve was blocked a few minutes later without difficulty. Paravertebral somatic nerve block was obtained by the medial route in the following two cases.

REPORT OF CASES

CASE 1.—This 54-year-old obese white woman had a painful left mid thigh stump following amputation for diabetic gangrene. The pain was constant and was aggravated by pressure, prohibiting the use of a prosthesis. Previous infiltration of the stump had given transient relief. Pain was localized in the distribution of the third and fourth lumbar nerves. Butethamine (monocaine®) hydrochloride in oil injected about these nerves by the medial route gave complete relief for two days. Accordingly

these nerves were each blocked with 2 cc. of 2% procaine hydrochloride solution, with immediate relief. Paresthesias were elicited on the first placement of each needle. At each nerve 2 cc. of absolute alcohol were injected. Complete relief lasted during the six months she was followed, and the patient was fitted meanwhile with a comfortable artificial leg.

CASE 2.—A 54-year-old physician suffered from intractable pain due to inoperable carcinoma of the gallbladder, with invasion of the liver and parietal peritoneum. The right 5th to 10th intercostal nerves were blocked by this method, using 4 cc. of isoamylhydrocupreine dihydrochloride in oil at each spinal nerve. Relief was complete, lasting three days. To avoid alcoholic neuritis, alcohol was not injected. Instead, the 6th to 10th intercostal nerves were sectioned in the posterior axillary line, giving relief until the lesion invaded the stomach three weeks later.

SUMMARY

A medial approach for paravertebral injection of spinal nerves is described. This technique depends on contacting the lamina of the vertebra with the needle and redirecting it laterally to the vicinity of the spinal nerve. The method has the following advantages: 1. The subarachnoid space is avoided almost entirely. 2. Localization is extremely accurate, since the bony landmark is very close to the nerve. 3. The technique is easy to perform and is less painful, even in obese patients. 4. Although it is still present, the possibility of causing pneumothorax is minimized.

193-40 McLaughlin Ave.

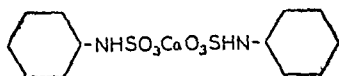
COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, M.D., Secretary.

Cyclamate Calcium.—Sucaryl Calcium (Abbott).— $C_{12}H_{21}CaN_2O_6S_2 \cdot 2H_2O$.—M.W. 432.57.—Calcium cyclohexylsulfamate.—The structural formula for calcium cyclohexylsulfamate dihydrate may be represented as follows:



Actions and Uses.—Cyclamate calcium is a synthetic sweetening agent for use in the diet of diabetics and other patients who must restrict their intake of carbohydrates. It may be used by patients on low sodium diets. Cyclamate calcium is essentially nontoxic, but an excessive intake may produce a laxative effect. This should be controlled by regulation of the amount used in the diet.

Dosage.—Cyclamate calcium is used in the form of a 15% solution for the preparation of foods or to sweeten beverages. 1.25 cc. (one-fourth teaspoonful) of a 15% solution is equivalent in sweetening power to about two teaspoonfuls of sugar (sucrose). A bitter taste becomes noticeable when the quantity in foods approaches 0.5%.

Tests and Standards.—

Physical Properties: Cyclamate calcium is a white, crystalline, practically odorless powder with a very sweet taste. It is freely soluble in water and practically insoluble in alcohol, benzene, chloroform and ether. The pH of a 10% solution is between 5.5 and 7.5.

Identity Tests: To 1 ml. of a 15% solution of cyclamate calcium, add 2 ml. of silver nitrate T.S. and mix: a white crystalline precipitate forms. To 2 ml. of a 15% solution of cyclamate calcium, add 1 ml. of 10% sodium nitrite, shake, and cautiously add sulfuric acid dropwise: a white precipitate forms.

Purity Tests: Determine the heavy metals content on 1 gm. of cyclamate calcium as directed in U.S.P. XIV, page 717: the turbidity developed does not exceed that of a control containing 20 γ of lead.

Dry about 1 gm. of cyclamate calcium, accurately weighed, for 4 hours at 130°: the loss in weight is not more than 9.5%.

Assay: (Nitrogen) Transfer to a semi-micro Kjeldahl flask about 0.1 gm. of cyclamate calcium, accurately weighed. Digest it with 7 ml. of sulfuric acid, 2.7 gm. of potassium sulfate and 0.3 gm. of mercuric oxide for 4 hours. Cool the contents of the flask and add 15 ml. of water. Make the solution alkaline with 40% sodium hydroxide and add 10 ml. of 40% sodium thiosulfate. Distill the ammonia into 20 ml. of 4% boric acid. Using a mixed indicator (1: 5 methyl red T.S. and bromocresol green T.S.), titrate the ammonia liberated with 0.05 N sulfuric acid. Each milliliter of 0.05 N acid is equivalent to 0.0007004 gm. of nitrogen and 0.009913 gm. of anhydrous cyclamate calcium. The amount of nitrogen present is not less than 6.93 nor more than 7.21%, equivalent to not less than 98.0 nor more than 102.0% of anhydrous cyclamate calcium.

(Calcium) Transfer to a 400 ml. beaker about 0.5 gm. of cyclamate calcium, previously dried at 130° for 4 hours and accurately weighed. Add 10 ml. of diluted hydrochloric acid and 15 ml. of ammonium oxalate T.S., and heat the mixture just to boiling. Add 25 ml. of ammonium hydroxide T.S., continue boiling for 5 min., allow the beaker to stand for 1 hour, then filter the mixture through a sintered glass crucible. Wash the residue with about 200 ml. of water. Transfer the crucible containing the precipitate back to the original beaker, add enough water to cover the crucible and 7 ml. of sulfuric acid, heat the material to 90° and then titrate with 0.1 N potassium permanganate. If the temperature of the solution falls below 70°, reheat it before continuing the titration. Each ml. of 0.1 N potassium permanganate is equivalent to 0.002004 gm. of calcium and 0.001983 gm. of anhydrous cyclamate calcium. The amount of calcium present is not less than 9.91 nor more than 10.3%, equivalent to not less than 98.0 nor more than 102.0% of anhydrous cyclamate calcium.

Dosage Forms of Cyclamate Calcium

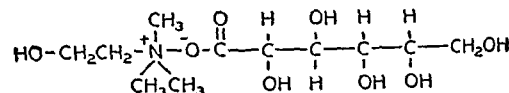
SOLUTION. **Identity Tests:** The solution responds to the identity tests described in the monograph for cyclamate calcium.

Assay: (Nitrogen) Transfer to a semi-micro Kjeldahl flask an accurately measured amount of the solution equivalent to about 0.1 gm. of cyclamate calcium. Continue as directed in the assay for nitrogen in the monograph for cyclamate calcium starting with, "... and digest it with 7 ml. of sulfuric acid ..." Each milliliter of 0.05 N acid is equivalent to 0.01081 gm. of cyclamate calcium dihydrate. The amount of cyclamate calcium dihydrate present is not less than 95.0 nor more than 105.0% of the labeled amount.

(Calcium) Transfer to a 400 ml. beaker an accurately measured amount of the solution equivalent to about 0.5 gm. of cyclamate calcium. Continue as directed in the assay for calcium in the monograph for cyclamate calcium starting with, "Add 10 ml. of diluted hydrochloric acid and 15 ml. of ammonium oxalate T.S. ..." Each milliliter of 0.1 N potassium permanganate is equivalent to 0.02163 gm. of cyclamate calcium dihydrate. The amount of cyclamate calcium dihydrate present is not less than 95.0 nor more than 105.0% of the labeled amount.

Solution Sucaryl Calcium: 118.3 cc. bottles. A solution containing 0.15 gm. of cyclamate calcium in each cubic centimeter. Preserved with 0.1% benzoic acid and 0.05% methylparaben. U. S. Patent 2,275,125. Abbott Laboratories, North Chicago, Ill.

Choline Gluconate.— $C_{11}H_{25}NO_8$.—M.W. 299.32.—2-(Hydroxyethyl)-trimethylammonium D-gluconate.—The structural formula of choline gluconate may be represented as follows:



Actions and Uses.—Choline gluconate has the same actions and uses as other salts of choline.

Dosage.—Adults: orally, 12 to 15 gm. daily in three divided doses. To provide the equivalent of 1 gm. of choline base, 2.46 gm. of choline gluconate is required.

Tests and Standards.—

The following tests and standards apply to a 95% sample of choline gluconate, which is commercially unavailable. The commercially available material is a 58 to 62% aqueous solution.

Physical Properties: Choline gluconate is a straw colored, highly viscous mass possessing an amine-like odor and a bitter taste. It is soluble in water, sparingly soluble in alcohol, very slightly soluble in ether, and practically insoluble in benzene and chloroform. The pH of a 50% solution is between 5.0 and 6.0.

Identity Tests: To 1 ml. of 10% choline gluconate add 5 ml. of mercuric potassium iodide T.S.: a pale yellow precipitate forms.

Add 1 ml. of 1% choline gluconate to 2 ml. of a cobaltous chloride solution (U. S. P. test solution diluted 1:25). Add 2 ml. of 2% potassium ferrocyanide: an emerald green color develops immediately.

To 1 ml. of ferric chloride T.S. add 1 ml. of 10% choline gluconate: an intensification of the yellow color occurs.

To 5 ml. of a 10% solution of choline gluconate add 0.5 ml. of glacial acetic acid and 1 ml. of freshly distilled phenylhydrazine. Heat on the steam bath for 30 min., allow the solution to cool and scratch the inner surface of the glass container: the crystals of gluconic acid phenylhydrazide formed, recrystallized twice from alcohol, melt between 199 and 202°.

Purity Tests: Accurately weigh about 0.5 gm. of choline gluconate and determine the water content by the Karl Fischer method (*U. S. P. XIV*, page 795). The amount of water present is less than 5%.

Ash about 1 gm. of choline gluconate, accurately weighed: the residue is less than 0.05%.

Assay: (Choline Gluconate) Accurately weigh about 0.2 gm. of choline chloride, *U. S. P. Reference Standard*, into a 100 ml. volumetric flask and make up to the mark with water. Transfer 4, 6, 8 and 10 ml. portions of the solution to separate test tubes, to each tube add 5 ml. of a freshly prepared and filtered saturated solution of ammonium reineckate (about 0.15 gm./5 ml.), shake the tubes and allow them to stand for 20 min. Filter the mixtures with suction, collecting the precipitates in fritted glass funnels. Wash the precipitates with 5 ml. portions of ice-cold water until the filtrates are colorless and then with two 2 ml. portions of ice-cold alcohol. Continue drawing air through the filter funnels until the precipitates are dry. Place test tubes under the stems of the funnels in the suction flasks and, with the aid of suction, wash the precipitates into the test tubes with three 5 ml. portions of acetone. Transfer the filtrates to 25 ml. volumetric flasks, rinse the test tubes with acetone, make up the solutions to 25 ml. with acetone and shake. Measure the light absorptions at 5260 Å. with a spectrophotometer, using acetone as a blank. Plot absorptions versus concentrations to give a standard curve. Accurately weigh into a 100 ml. volumetric flask about 0.3 gm. of choline gluconate and dilute to the mark with water. Transfer 10 ml. of the solution to a test tube and proceed as before. Read the concentration of choline chloride from the standard curve. Each gram of choline chloride is equivalent to 2.144 gm. of choline gluconate. The amount of choline gluconate present is not less than 95.0 nor more than 105.0%.

Dosage Forms of Choline Gluconate

SOLUTION (58-62%). **Assay:** From 10 ml. of the choline gluconate solution prepare an aqueous solution whose final concentration is about 3 mg. per milliliter. Transfer 10 ml. of this solution to a test tube and carry out the spectrophotometric determination described in the monograph for Choline Gluconate starting with, "... add 5 ml. of freshly prepared and filtered saturated solution of ammonium reineckate ..." The amount of choline gluconate present is not less than 90.0 nor more than 110.0% of the labeled amount.

Solution Choline Gluconate: 473 cc. bottles. A flavored solution containing 0.62 gm. of choline gluconate in each cubic centimeter. Commercial Solvents Corporation, New York.

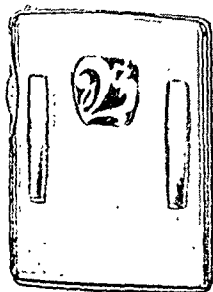
COUNCIL ON PHYSICAL MEDICINE AND REHABILITATION

The Council on Physical Medicine and Rehabilitation has authorized publication of the following reports.

RALPH E. DE FOREST, M.D., *Secretary.*

MICROTONE HEARING AID, MODEL T612, ACCEPTED

Manufacturer: The Microtone Company, Ford Parkway on the Mississippi, St. Paul 1.



Microtone Hearing Aid, Model T612

The Microtone Hearing Aid, Model T612, an electrical instrument with air conduction receiver, measures (excluding hinge, clothing clip, and control) 73 by 57 by 20 mm. and weighs 82 gm. With batteries, receiver, and cord, the total weight is 150 gm.

The instrument was tested in a laboratory acceptable to the Council and was found to satisfy the minimum requirements of the Council for acceptance of hearing aids. The Council on Physical Medicine and Rehabilitation voted to include the Microtone Hearing Aid, Model T612, in its list of accepted devices.

UNEX HEARING AIDS, MODELS 200 AND 230, ACCEPTED

Manufacturer: Nichols and Clark, Hathorne, Mass.

The Unex Hearing Aids, Models 200 and 230, are electric hearing aids housed in metal cases. The smaller, Model 200, measures 53 by 40 by 18 mm. without the clothing clip. The complete assembly with batteries, cord, and receiver weighs 73.5 gm. The



200



230

Unex Hearing Aids, Models 200 and 230

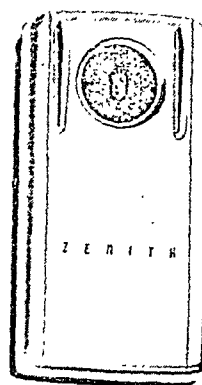
larger, Model 230, measures 69 by 40 by 18 mm., and the assembly with batteries, cord, and receiver weighs 91 gm. Like many other recent instruments, the Unex dispenses with a tone control.

Tests in a laboratory acceptable to the Council gave evidence that this instrument satisfied the minimum requirements of the Council for acceptance of hearing aids. The Council on Physical Medicine and Rehabilitation voted to include the Unex Hearing Aids, Models 200 and 230, in its list of accepted devices.

ZENITH HEARING AID, MODEL "SUPER-ROYAL," ACCEPTED

Manufacturer: Zenith Radio Corporation, 5801 W. Dickens Ave., Chicago, 39.

The Zenith Hearing Aid, Model "Super-Royal," is an electrical instrument conventional in shape and design but designed for wearers with severe impairments of hearing who need and can tolerate a high acoustic output. It is equipped for both air and bone conduction. Its dimensions, excluding clothing clips, are 113 by 59 by 23 mm. With batteries, cord, and receiver it weighs 251 gm.



Zenith Hearing Aid, Model "Super-Royal"

Evidence from tests in a laboratory acceptable to the Council showed that this instrument performed as represented by the manufacturer and that it satisfied the minimum requirements of the Council for acceptance of hearing aids. The Council on Physical Medicine and Rehabilitation voted to include the Zenith Hearing Aid, Model "Super-Royal," in its list of accepted devices.

CLEARTONE HEARING AID, MODEL 700, ACCEPTED

Manufacturer: American Sound Products, Inc., 1303 S. Michigan Ave., Chicago 5.

The Cleartone Hearing Aid, Model 700, is an electrical instrument housed in a metal and plastic case that measures 20 by 64 by 65 mm. It has air conduction or bone conduction earphones. With plastic-coated cord and with batteries, the assembly weighs 167 gm.

Tests in a laboratory acceptable to the Council showed that this instrument satisfied the Council's minimum requirements for acceptance of hearing aids. The Council on Physical Medicine and Rehabilitation voted to include the Cleartone Hearing Aid, Model 700, in its list of accepted devices.

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TRANSMISSIBLE LEUKEMIA IN MICE

Gross¹ of the Veterans' Administration Hospital, Bronx, N. Y., reports experimental evidence suggesting that "spontaneous" leukemia in mice is a virus disease. He had available for these experiments two different inbred strains of mice, one of which was essentially free from the disease. Through 16 generations this strain had not shown a single case of leukemia, while in 70% of the females of the second strain "spontaneous" leukemia developed after the mice were 7 months of age.

In a typical experiment, fragments of spleen and enlarged lymph nodes of the leukemic mice were emulsified in 4 vol. of isotonic salt solution and then centrifuged for 15 minutes at 3,000 rpm. Newborn young of the nonleukemic strain less than 12 hours old were each given injections subcutaneously or intraperitoneally with 0.1 cc. of the resulting supernatant fluid. Of 14 young mice thus injected, leukemia developed in 7 at 8 to 11 months of age, and 5 others died later of leukemia.

In a refinement of this technique, samples of the leukemic supernatant fluid were passed through a Seitz filter. The resulting filtrate was injected subcutaneously in 0.1 cc. doses into 25 nonleukemic suckling mice less than 12 hours old. In 7 of these, "spontaneous" leukemia developed at 6½ to 9 months of age; the 18 remaining mice, now 7 to 9 months old, are still under observation.

Tests were also made of the possibility of transplacental transmission of the leukemic agent. Five pairs of mice of the nonleukemic strain were given injections during infancy with the filtrable agent and afterward mated during early adult life. Of these 10 mated adults, leukemia subsequently developed in 7. Of the 27 offspring born to these preleukemic parents, 13 died of leukemia at 14 to 20 months of age. The latent leukemia agent in the tissues

1. Gross, L.: "Spontaneous" Leukemia Developing in C3H Mice Following Inoculation, in Infancy, with AK-Leukemic Extracts, or AK-Embryos, *Proc. Soc. Exper. Biol. & Med.* 76:27 (Jan.) 1951; Pathogenic Properties, and "Vertical" Transmission of the Mouse Leukemia Agent, *ibid.* 78:342 (Oct.) 1951.

1. Debré, R., and others: *La maladie des griffes de chat*, Semaine hôp. Paris 26: 1895-1904 (May 30) 1950.

2. Mollaret, P.; Reilly, J.; Bastin, R., and Tournier, P.: Sur une adénopathie régionale subaiguë et spontanément curable, avec intradermo-réaction et lésions ganglionnaires particulières, *Bull. et mém. Soc. méd. hôp. Paris* 66: 424-449 (March 24-31) 1950.

3. Mollaret, P.; Reilly, J.; Bastin, R., and Tournier, P.: Documentation nouvelle sur l'adénopathie régionale subaiguë et spontanément curable décrite en 1950: La lymphoréticulose bénigne d'inoculation, *Presse méd.* 58: 1353-1355 (Dec. 2) 1950.

4. Lemaire, A., and Debray, J.: Sur une épidémie familiale d'adénite subaiguë bénigne de nature inconnue, *Bull. et mém. Soc. méd. hôp. Paris* 66: 375-378 (March 10-17) 1950.

of the young adult parents was therefore transferred in effective doses to the unborn young.

The simplest means of explaining these findings would be to assume that "spontaneous" leukemia in mice is a virus disease, which remains latent during vigorous early adult life. Another theory might picture the leukemic agent as causing mutation of certain embryonic or early postembryonic tissue cells.

CAT SCRATCH DISEASE

Debré and his associates¹ reported in 1950, under the title "La maladie des griffes de chat," a hitherto undescribed clinical entity. The disease was seen most frequently in children and occasionally in adults. It was characterized by subacute lymphadenitis which frequently suppurated and healed without a scar. The course of the disease was usually mild but occasionally, particularly in adults, was accompanied by mild fever and painful adenopathy. The adenopathy was usually preceded by a small maculovesicular skin lesion. The patients often had a history of being scratched by a cat. Microscopic studies of the involved lymph node revealed formation of nodules composed of reticular cells and of a central necrosis. Attempts at identifying the causative agent have been unsuccessful. The infection apparently was not caused by bacteria or spirochetes, nor did it appear to be an anomalous type of tularemia or of lymphogranuloma venereum, both of which it resembled very closely.

At about the same time Mollaret and his associates² at the Claude Bernard Hospital in Paris reported eight similar cases. Somewhat later Mollaret and co-workers³ reported on 42 cases of their own and on 58 cases gathered from various cities in France. Histological studies made by this group revealed the process as a reticular hyperplasia, which may remain stationary or regress, and which frequently progresses to formation of necrotic foci and microscopic abscesses and to suppuration with periadenitis and formation of abscesses. Mollaret considered the disease to be essentially a benign reticulocytosis caused by inoculation. The disease was seen sporadically and at times as a small familial epidemic. Thus Lemaire and Debray⁴ reported five cases occurring in a family of six, and the Mollaret group recorded a similar familial incidence. The family had a cat in the Lemaire and Debray group but there was no history of scratches. Of the 42 cases reported by Mollaret and his associates,³ in only 19 was there a history of a cat scratch, and 2 were bitten by a cat. In one patient there was a history of a puncture of the skin by a fragment of bone, one suffered a skin abrasion while dressing a pig; in one an abrasion was caused by a thorn, and in another by a splinter of wood. In five there was a cat on the premises but no history of scratching, while in eight instances there was no contact whatsoever with a cat. The fact that veterinarians have not seen this disease in cats and that intradermal tests with the particular antigen are negative suggests that the role of the cat in the infection is a passive one. The particular virus, according to Mollaret, is probably widely distributed in plants and vegetable life.

The disease is frequently confused with tuberculous cervical adenitis, tularemia, lymphogranuloma venereum, infectious mononucleosis, sarcoidosis, sodoku, and Hodgkin's disease. The adenopathy is oftener single than multiple and is always unilateral. It usually resolves itself in a few weeks whether treated or not. The blood picture does not undergo much change. There is no involvement of viscera and the spleen is not enlarged. Aureomycin and terramycin appear to be effective in shortening the course of the disease and in preventing suppuration of involved nodes. Mollaret, however, expresses doubt as to effectiveness of the antibiotics, because some mild cases do not go on to suppuration, even when not treated.

This particular clinical entity was recognized in this country by Foshay of Cincinnati about 20 years before the above-mentioned workers. In the course of his studies of tularemia Foshay had recognized this particular entity and had even prepared an antigen from the pus of an involved lymph node that gave positive reactions on intradermal injection. This antigen was prepared according to the principles of the Frei test for lymphogranuloma venereum. Foshay did not report these observations; however, he had informed Debré of his discoveries when the latter visited the United States in 1947 and had given him a supply of his antigen.

Hanger and Rose of New York have prepared a similar antigen from pus aspirated from a paronychia Hanger had contracted while gardening. There was a cat in the household but no history of a scratch. The paronychia was followed later by a suppurative regional adenitis accompanied with fever and constitutional symptoms. The antigen prepared from the pus gave an intense intradermal reaction in Hanger and also in patients previously studied by Foshay.

Greer and Keefer⁵ reported one case in which there was a history of a cat scratch. In the 12 patients reported by Daniels and MacMurray,⁶ there was a history of more or less intimate contact with cats; 7 patients had been scratched and 1 was bitten. Five of the patients had a primary lesion at the site of inoculation. The lymphadenopathy was evident in 18 to 21 days after the development of the initial lesion. The course of the disease was mild. There were chills or chilliness, headache, and generalized aching in some of the patients. The Hanger-Rose test was positive in all. The antigen material was supplied by Foshay, Mollaret, and Debré. The intradermal test was negative in the contacts. Patients with lymphogranuloma venereum, Hodgkin's disease, leukemia, tuberculous cervical adenitis, and tonsillitis with cervical adenopathy all gave negative responses to the intradermal test.

Mollaret and his collaborators⁷ have announced in a recent communication the discovery of the particular virus causing the disease. They have succeeded in transmitting the disease to one out of four volunteers. They have further succeeded in transmitting the disease to *Cercopithecus ethiops sabeus* monkeys by intracutaneous inoculation of emulsions made from infected lymph nodes from two patients. The animals showed a primary lesion at the site of injection in 28 to 54 days and enlarged regional lymph nodes in 36 to 63 days after

inoculation. The intradermal reaction was positive in 48 hours in one monkey on the 64th day after infection. Histological studies of the skin lesions and of the lymph nodes in both man and monkeys revealed, when stained with Giemsa stain, basophilic granules within reticulocytes, plasma cells, and lymphocytes. These granules were somewhat smaller than the eosinophilic and basophilic granules ordinarily seen. They were numerous in early lymph node lesions, particularly in the reticulocytes bordering on a necrotic zone. Mollaret considers these "granulocorpuscles" a visible form of the causative virus. These interesting observations require further study for their confirmation.

CORTISONE IN MYOCARDIAL INFARCTION

Johnson and co-workers¹ have reported that the administration of cortisone following ligation of a branch of the coronary artery in dogs results in a pronounced decrease in the size of the myocardial infarct produced. In their experiment the anterior descending branch of the left coronary artery was ligated just below the origin of the circumflex branch in 14 dogs. Seven of these animals were given cortisone in doses of 12.5 to 20 mg. twice daily for 14 to 22 days, starting on the day of ligation. The remaining seven received no cortisone. Two or three weeks after operation the hearts of all the animals were examined grossly and microscopically. In the cortisone-treated animals the infarcts were approximately 1/7 the size of those in the control animals. Microscopically, the infarcts in the cortisone-treated animals showed a decrease in fibroblastic proliferation and a sharp line of demarcation between the damaged and healthy myocardium. Moreover, the degree of cardiac embarrassment during life, as gaged by fatigability, loss of appetite, and loss of interest in surroundings, was significantly less in the treated dogs than in the controls. While the doses of cortisone used reduced the number of postoperative pericardial adhesions, they did not interfere with wound healing. Further studies are being carried out to determine the late results of cortisone administration in experimental coronary occlusion.

Whether these observations have clinical application in man remains to be demonstrated. The use of cortisone in patients with myocardial infarction would involve some risk because of the tendency of this compound under certain circumstances to produce retention of sodium and water, thus increasing the load on the heart. This hazard, along with those of aggravating preexisting hypertension or of increasing a tendency to thrombosis, would have to be balanced against any potential benefit to be derived from the drug.

5. Greer, W. E. R., and Keefer, C. S.: Cat-Scratch Fever: A Disease Entity, *New England J. Med.* 244: 545-548 (April 12) 1951.

6. Daniels, W. B., and MacMurray, F. G.: Cat-Scratch Disease: Non-bacterial Regional Lymphadenitis, *A. M. A. Arch. Int. Med.* 88: 736-751 (Dec.) 1951.

7. Mollaret, P.; Reilly, J.; Bastin, R., and Tournier, P.: La découverte du virus de la lymphoréticulose bénigne d'inoculation: Inoculation expérimentale au singe et colorations, *Presse méd.* 59: 701-704 (May 23) 1951.

1. Johnson, A. S.; Scheinberg, S. R.; Gerisch, R., and Saltzstein, H. C.: Effect of Cortisone on Experimentally Produced Myocardial Infarction, *Harper Hosp. Bull.* 9: 187 (Nov.-) 1951.

ORGANIZATION SECTION

STATEMENT BY THE BOARD OF TRUSTEES

NATIONAL DOCTORS COMMITTEE FOR IMPROVED FEDERAL MEDICAL SERVICES

It is apparent from a recent influx of correspondence inquiring about the activities of the National Doctors Committee for Improved Federal Medical Services that the position of the American Medical Association with regard to the medical recommendations of the Hoover Commission requires amplification.

Individual physicians in the United States and, more recently, their wives have received letters and brochures from the Doctors Committee, an affiliate of the Citizens' Committee for the Hoover Report. These letters urge individual and collective political pressure to force hearings on legislation pending in the Congress that would effect the medical recommendations of the Hoover Commission. In some instances it has been assumed that the American Medical Association is joining in this effort. This is not the case.

During the 81st Congress a bill (S. 2008) was introduced that sought to accomplish the medical recommendations of the Hoover Commission. Dr. Walter B. Martin, a member of the Board of Trustees, testified on behalf of the American Medical Association in opposition to this bill before the Senate Committee on Labor and Public Welfare, on July 11, 1950.

Substantially similar bills (S. 1140 and H. R. 3688) were introduced in the 82d Congress to carry out the same purposes as embodied in S. 2008, 81st Congress. On April 13, 1951, the Committee on Legislation of the American Medical Association voted to disapprove these measures. This action was later approved by the Board of Trustees.

In response to an invitation from the National Doctors Committee, representatives of the American Medical Association met with representatives of that committee and others in New York in June 1951, for the purpose of reconciling the divergent views concerning this legislation. At that conference representatives of the National Doctors Committee indicated orally that they would be agreeable to suggested amendatory legislation that would incorporate the majority of the suggestions presented by the American Medical Association. A revised bill was subsequently prepared and submitted to the Association for consideration.

After a careful study of the substitute proposal, the Committee on Legislation voted to oppose the measure at its meeting in Los Angeles, Dec. 4, 1951. The Committee noted that, while certain minor changes suggested by the Association had been made, the revised bill still provided for the transfer to the new department of health of the military and Veterans Administration hospitals—a transfer opposed by the American Medical Association.

The Board of Trustees on Dec. 6, 1951, approved the action of the Committee on Legislation and again reiterated its hope that economy could be effected in the operation of the federal medical services. It restated its belief that such economy could be best accomplished by coordination of the several hospital systems, providing for joint use of available beds and joint planning in the field of hospital construction, and that a central hospital board with authority to adjust the hospital program to the needs of the services could gain the end desired without a consolidation of professional personnel.

The disagreements between the Association's position and either S. 1140 or the alternative measure proposed by the Doctors Committee are basic and divergent.

NEW SURVEY OF COLLEGE HEALTH SERVICES

In 1936, the Bureau of Medical Economics (Rosco G. Leland M.D., Director) of the American Medical Association reported the results of a comprehensive survey of the health services of 255 colleges and universities in a 187-page book, "University and College Student Health Services." This survey concerned the nature and extent of health programs, their origin and growth, present status, and certain related problems.

The results of a second survey of college health services have recently been published as Bulletin 88 of the Bureau of Medical Economic Research of the American Medical Association. This study, "Second Survey of University and College Health Services: 1949-1950," is based on returns from 462 colleges of the 1,124 to which questionnaires were sent in May, 1950, requesting data for the academic year 1949-1950. A copy of Bulletin 88 may be obtained from the Bureau of Medical Economic Research, American Medical Association, 535 N. Dearborn St. Chicago 10.

Great variation was noted in the services, personnel, and facilities available to students in these colleges; this may be largely due to the differing needs of students in varying types of colleges and communities. Data on routine health examination, medical treatment for ambulatory and bed patients, surgery, and special services are reported by sex and number of students admitted, type of control, and staff of health service. It was found that the larger colleges provided more inclusive health services for their students, probably because these colleges more frequently had at least one full-time physician on the health service staff.

Services for faculty and other employees were rarely reported. Only 37% of the colleges reported care for ambulatory patients. Since most of the faculty and other employees are living in their own homes and are often protected by private or college sponsored health insurance plans, their health needs are frequently met outside the scope of the college health service itself; rather, they are treated as citizens of the community in which they reside.

Student health services are usually financed by a separate fee or by a fee included in tuition or student fees. Required insurance by an outside carrier was rarely reported. Seventeen colleges required insurance of students, and 52 colleges offered it as optional. Insurance was required of faculty in five colleges and of other employees in three colleges. Optional insurance coverage is available to faculties of 147 colleges and to other employees of 114 colleges.

The college health service influences the student's concepts of the importance of good medical care through contacts with the health service personnel and the utilization of the facilities provided. Many students receive these health services through the operation of some kind of prepayment "health insurance plan" to which the student contributes a part of the cost through the payment of fees to the college. This experience may influence his later concepts of the costs of medical care and his evaluation of the merits of various types of health insurance. The college health service is, therefore, an educational influence.

Although this study is incomplete, it should be of interest to college administrators, health service personnel, and physicians, particularly those living in college communities. It is the responsibility of these persons to evaluate the obligations of the college health service to the students, faculty, and other employees.

STATE MEDICAL LEGISLATION

Arizona

Bills Introduced.—H. C. M. 1, proposes to direct the Arizona legislature to request federal legislation to make available to the state of Arizona sufficient federal funds to adequately provide hospitalization and care of persons from other states who come to Arizona seeking relief from tuberculosis. H. 190, proposes to provide for the appointment of a director of the state department of health, such person to be a reputable physician licensed to practice in the state, a holder of a degree of doctor of medicine from a medical school recognized by the Council on Medical Education and Hospitals of the American Medical Association, and a person of at least five years' experience in full-time administration of a department of public health or three years' experience plus a degree from an accredited school of public health.

Kentucky

Bills Introduced.—S. 128, proposes to authorize a coroner to perform an autopsy when necessary or to appoint a physician to perform such autopsy. S. 140, proposes the creation of a department of mental health and sets forth the powers, duties and functions of such a proposed department.

Bill Enacted.—H. 62 was approved February 7, 1952. It amends the Kentucky law relating to narcotic drugs by providing, among other things, that any person who sells, administers or dispenses narcotic drugs to persons under 21 years of age shall be guilty of a felony.

Michigan

Bills Introduced.—H. 358, proposes to repeal the basic science law. S. 251, proposes to amend the basic science law, by among other things, eliminating hygiene and public health from the list of basic science subjects and by exempting interns and residents who are training in Michigan hospitals from the operation of the law.

Mississippi

Bills Introduced.—H. 228, proposes the enactment of a modern rabies control law. H. 272, proposes that applicants for drivers license shall furnish a certificate from a licensed physician, registered nurse, or reputable hospital as to his blood type and proposes that such blood type be entered on the person's driver's license when issued. S. 268, proposes to authorize the board of trustees of state institutions to provide nursing scholarships for student nurses.

New York

Bills Introduced.—A. 840, A. 1110, S. 1054 propose the creation of a temporary state commission to make a comprehensive study and investigation of all of the problems arising from or in connection with the care, protection, and treatment of mentally ill persons in public and private hospitals and institutions, with special emphasis on the need for the use of jackets and other mechanical restraints presently used and other techniques and practices presently employed in connection with the care and treatment of such patients with the view and for the purpose of recommending the abolition of the use of such jackets and restraints, if found feasible, and for the purpose of recommending such improvements and such techniques and practices as may be deemed necessary. A. 848, proposes the creation of a temporary commission to investigate and study the need for an annual health examination of each resident of the state. A. 1030, and S. 899 to amend the mental hygiene law, propose, among other things, that no person, association or corporation shall establish or maintain an institution for the care, custody or treatment of persons who are mentally incompetent without first obtaining a license therefor. A. 842, A. 1111, S. 1058 propose to direct the department of mental health to conduct mental health research programs. A. 1214, to amend the physiotherapy law, proposes to authorize applicants for a license to practice physiotherapy to temporarily practice such activities for a period of six months during the pendency of their application for a license. A. 1234, proposes to require every physician to immediately give notice to the health officer of the county, city, town or village where the patient resides of every case of cancer or other malignant tumor under his care. A. 1394 and S. 1173 propose the establishment of 50 state scholarships to be awarded to registered professional nurses for the purpose of advanced education in teaching or administration of nursing. A. 1405 and S. 1174 propose the creation of 500 scholarships to attendants at schools of nursing approved by the Regents for the training of registered professional nurses. A. 1436 and S. 1322 propose that physicians who are on the staff of and actually perform services as often as twice monthly at a free clinic, dispensary or outpatient unit operated by or affiliated with a hospital maintained in whole or in part by a municipality of the state, may have an additional personal exemption of \$2,500, so far as his individual income tax return is concerned. A. 1446 and S. 1493 to amend the workmen's compensation law, propose to require physicians and medical consultants to furnish to claimants, or their authorized representatives, copies of every report of examination, finding and opinion made by such physician and medical consultant with respect to the claimant. A. 1647, to amend the education law, proposes the creation of a state board of physiotherapy examiners. A. 1723, proposes that no person, firm or corporation owning and operating a hospital shall permit the use of an ambulance for the transportation to such institution of sick or wounded persons unless there is in attendance upon such ambulance at all times a duly qualified physician or intern who is a member, or connected with the staff, of the institution. A. 1731 and S. 1477, to amend the education law, proposes the creation of a state board of chiropractic examiners

and defines chiropractic as the science of locating and the removing of nerve interference of the human body according to chiropractic principles where such interference is the result of or related to misalignment of subluxations of the vertebral column. It excludes operative surgery, the reduction of fractures, the prescription or use of drugs or medicines, and the practice of obstetrics. A. 1796 and S. 1594 propose that every membership corporation maintaining a hospital, infirmary, dispensary, or the like, shall be liable for damages for personal injuries alleged to have been sustained by any person by reason of the negligence or malpractice of a physician, surgeon, or nurse while engaged in practicing his profession in such institutions. A. 1977, proposes to direct the fluoridation of public water supplies and storage reservoirs after consultation with the commissioner of health and recognized medical and dental authorities. A. 2003 and S. 1700 propose to make municipal corporations liable for the malpractice of resident physicians, interns and other licensed physicians rendering services without compensation in a public institution or in the course of a home care service maintained by such institution. A. 2255 and S. 1608 propose to authorize the state comptroller to contract for the furnishing of medical and surgical services and hospital services for state employees. A. 2270, proposes regulations for the licensing of operators of shoe fitting fluoroscopy apparatus. A. 2288, proposes to make it unlawful for any public or semipublic hospital to refuse to permit any physician or surgeon duly licensed in the state to diagnose, treat or operate on any patient in such hospital or refuse admission to any such hospital of any patient who has been recommended to be sent to or has been sent to such hospital by any such physician or surgeon. S. 778, proposes the creation of a consumers bureau in the state department of health for the purpose of protecting the consumer in the manufacture and sale of adulterated or misrepresented food, drugs, cosmetics, or health devices. S. 1037, proposes that any person who has been granted a license by the state of New York to practice a profession who, upon being called before a grand jury to testify concerning any of his professional acts not covered by the laws of professional secrecy, refuses to sign a waiver against subsequent criminal prosecution or to answer any relevant questions concerning such matters shall forfeit his professional license and the same shall be revoked forthwith by the licensing authority at the suit of the district attorney at whose instance the person was called before the grand jury. S. 1082, proposes to authorize subscribers to medical care plans to have the choice of any duly licensed physician, whether or not such physician is designated or approved by the corporation. The proposal would further require that all duly licensed physicians would be eligible to participate in the plan. S. 1185, proposes to require that any hospital which is not properly equipped and staffed with a resident anesthetist, for the purpose of administering anesthetics at all times, shall be ineligible to receive any payment for hospital care or medical expense indemnity from a nonprofit hospital service corporation, notwithstanding any other provision of the law. S. 1214, proposes to prohibit the refilling of any prescription for a barbiturate or any other hypnotic or somnifacient drug unless the prescription includes a statement by the prescriber that it may be refilled and specifying the minimum interval between fillings and the total number of refillings prescribed. S. 1390, to amend the labor law, proposes to require every trade, industry or occupation wherein fifty or more persons are employed to establish a first-aid station under the charge of a competent person whose sole duty shall be to provide aid for injuries received during employment. S. 1544, proposes the creation of a committee to make studies and carry into effect a program of research to aid in finding a cure for poliomyelitis. S. 1550, to amend the education law relating to eye and ear tests of school children, proposes that such tests be made twice rather than once each year and that reports of defects be referred without delay to the principal of the school and the parents of the child. S. 1587, proposes to exempt from taxation property belonging to a medical or dental society. S. 1614, to amend the public health law, proposes regulations for the care, treatment, guidance and rehabilitation of narcotic drug users. S. 1675, proposes regulations for the conduct of public hospitals and provides, among other things, that it shall be unlawful for any hospital corporation to be the vendor of medical diagnosis or treatment. Such hospitals, however, may employ physicians under a contract or salary arrangement for the rendition of medical care to patients only when such diagnosis and treatment is a public charge. In all other cases the medical diagnosis shall be rendered to patients independently of any hospital charges and under contractual relationship between the patient and the physician. S. 1739, proposes to require chauffeurs or operators, before having their license renewed to present a certificate from a duly licensed physician attesting that the applicant has been examined and found mentally and physically competent to operate a motor vehicle. S. 1753, proposes that the officers, superintendents, and the like which refuses to employ a physician, intern, or nurse or permit such person to use the hospital facilities solely because of race, color, creed, or religion shall be guilty of a misdemeanor. S. 1975, proposes the creation of a temporary commission to study the feasibility of having a free choice of physicians in any nonprofit medical, dental, indemnity, or hospital service corporations plan. S. 1997, proposes an appropriation to the department of health for the purpose of conducting experiments in co-operation with the medical society of New York State and mass detecting diseases through the process of multiphasic screening. S. 2005, proposes regulations for the control of nurses' registries.

Bill Enacted.—S. 277 has become Chapter 8 of the Laws of 1952. It provides regulations for the compulsory care, treatment, guidance, and rehabilitation of adolescent drug users.

Pennsylvania

Bill Introduced.—S. 883, proposes to authorize the issuance of chiropractic licenses by the state board of chiropractic examiners to certain persons who hold licenses in drugless therapy, under certain circumstances.

MEDICAL NEWS

CALIFORNIA

Symposium on Infertility.—This symposium will be given at the regular meeting of the San Francisco Medical Society in its headquarters building March 4, at 8:15 p. m. Physicians speaking by invitation are Dr. Ernest W. Page, associate professor of obstetrics and gynecology at the University of California Medical School, Berkeley, and Dr. Juan F. Aycinena, clinical instructor in surgery (urology), Stanford University School of Medicine, San Francisco.

Dr. Geiger Leaves San Francisco.—After about 20 years of service as director of public health of the City of San Francisco, Dr. Jacob C. Geiger has resigned effective March 1 to undertake similar work in the department of public health in the city of Oakland. The San Francisco Medical Society credits him with having developed one of the most efficient emergency systems in the United States. Dr. Geiger also developed an outstanding ambulance service, placing ambulances in strategic positions throughout the city so they would be available within a few minutes to meet emergencies. He developed a two-way radio system in these ambulances. He had under his supervision about 2,350 public health department employees. Dr. Geiger was responsible also for the operation of hospitals connected with the city, in which there are about 4,000 beds.

DISTRICT OF COLUMBIA

Grants for Care of Advanced Cancer Patients.—George Washington University has received from the Alexander and Margaret Stewart Fund two grants designed to help and comfort persons suffering from incurable cancer. One grant of \$25,000 was awarded for home care of patients too ill to come to the clinic for treatment but not ill enough to require hospital care. An additional \$20,184 has been awarded for research to evaluate methods of treating cancer patients who are beyond help by routine surgical or x-ray therapy. Both grants will continue projects in progress previously supported by the Stewart Fund at The George Washington University Cancer Clinic under the direction of Dr. Calvin T. Klopp. Under the home care program patients able to pay and those unable to pay for service receive visits from physicians and nurses, necessary medicines, appliances and housekeeping aid arranged for by the clinic's social service worker.

ILLINOIS

Mumps in Illinois.—Among the more prevalent of the communicable diseases in Illinois at present is mumps, according to the State Department of Public Health. From 300 to 400 cases are currently being reported in the state each week. Out of a total of 858 cases recorded up to Jan. 19, only 230 were from Chicago. Ordinarily from 6,000 to 8,000 cases occur in Illinois each year.

Chicago

Society News.—At the annual meeting of the Chicago Dermatological Society in January Dr. James R. Webster, was elected president, Dr. John M. McCuskey, Peoria, vice-president, and Dr. Irene A. Neuhauser, secretary-treasurer.

Grants for Research.—The Hektoen Institute for Medical Research of the Cook County Hospital has received a grant of \$4,428 from the U. S. Public Health Service for a cancer control project entitled "Investigation as to the Incidence of

Operable Carcinoma of the Stomach at Autopsy" under the direction of Dr. Frederick Steigmann. A grant of \$12,420 was also received from the Commercial Solvents Corporation for the study of rheumatoid arthritis. This work will be done under the supervision of Dr. Eugene F. Traut and associates.

Progress Report on the Medical Center.—Construction of new facilities now nearing completion has increased the investment in the 305-acre medical center district on Chicago's Near West Side to \$155 million, \$55 million more than five years ago, according to Dr. Walter H. Theobald, president of the medical center commission. Present facilities include three medical schools, two dental schools, two schools of nursing, a school of pharmacy, a graduate college, a postgraduate school of medicine, a school of mortuary science, three hospitals, and five institutes and laboratories devoted primarily to research. Nine new projects are under construction: (1) the 500-bed Veterans Administration hospital and the Veterans Administration regional office building, (2) the 489-bed Chicago State Tuberculosis Sanitarium, (3) the 411-bed addition to the University of Illinois Research and Educational hospitals, (4) the 15-story Cook county interns and residents dormitory, (5) the 16-story Presbyterian Hospital School of Nursing, which will provide facilities for 350 graduate and student nurses, (6) the medical center steam plant already in operation, (7) the Cook County Graduate School of Medicine, a non-profit teaching establishment, (8) the University of Illinois staff apartment building, providing 145 apartments, and (9) the University of Illinois student residence hall, with facilities for 420 students.

The new east unit of the Dentistry-Medicine-Pharmacy Building at the University of Illinois and the residential unit for mentally ill children will be erected by the state department of public welfare early in 1952. Among the projects contemplated are the Stritch School of Medicine and the Dental School of Loyola University, which will include a teaching hospital, a research institute, and a student residence; Chicago Medical School, including its teaching hospital and a research laboratory, and the new east pavilion of Presbyterian Hospital. Plans are being drawn and sites have been selected for other types of medical services, which may be utilized for research and teaching purposes. These include an outpatient clinic for Cook County Hospital, the Morrison Home for the Aged, providing for research studies in geriatrics, the Chicago Foundlings Home, University of Illinois School of Nursing, the Institution for Tuberculosis Research, the Illinois Eye and Ear Infirmary, a psychiatric hospital and clinic for treatment of acute mental illnesses, the Cancer Research Institute, and an institute for research on alcoholism and drug addiction. When completed, the medical center district will represent an investment of \$300 million in land, building, equipment, and endowment.

INDIANA

Personal.—A year's leave of absence has been granted Dr. Donald J. Caseley, medical director of the Indiana University hospitals, Indianapolis. Dr. Caseley has been named as associate director of the Commission on Financing of Hospital Care.

Orthopedic Travel Club.—Indiana University, Indianapolis, was host to a group of orthopedic surgeons, known as the Orthopedic Travel Club the week end of Feb. 1. The surgeons came from various parts of the United States for their annual meeting here.

Radiologic Conferences.—Dr. Joseph L. Morton, Columbus, Ohio, radiologist for the Ohio State University hospitals, was a guest speaker on the medical center campus, Indianapolis, Feb. 21-22, for a series of conferences arranged by the department of radiology of the Indiana University School of Medicine with the support of the Indiana Cancer Society.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

KANSAS

State Opens Child Psychiatric Clinic.—Topeka State Hospital is ready to screen, diagnose, and treat on an outpatient basis any Kansas child needing psychiatric help. Additional facilities for boys and girls who need to be treated in the hospital for some period of time will be available in a few months. A new outpatient service for adults is also open to any Kansan on an appointment basis. Parents may take their children to the outpatient clinic in much the same way they would go to their family doctors after calling or writing for appointments. Probate judges and social and other referring agencies may also make use of this new service. The charge for any patient is on the basis of ability to pay.

MASSACHUSETTS

Dr. Bakst Succeeds Dr. Fleming.—Dr. Henry J. Bakst, associate professor of preventive medicine, has been promoted to full professorship and head of the genital infection department of Boston University and of the Massachusetts Memorial Hospitals. Dr. Bakst takes up his new duties on the resignation of Dr. William L. Fleming, who recently accepted the post of professor of preventive medicine at the University of North Carolina, Chapel Hill.

Training Public Health Personnel.—The position of director of training, Massachusetts Department of Public Health, has been made a part of the permanent administration of the department. Until now, the position has been financed by a grant from the W. K. Kellogg Foundation, one of the funds supporting the department's program of training public health personnel. Leon A. Bradley, Ph.D., who has been director of training since the division was created in 1950, will continue in that position. The division has trained 310 public health workers in medical health administration, medical social work, public health nursing, health education, and environmental sanitation.

MICHIGAN

Residencies in Ophthalmology.—Residencies in ophthalmology are available immediately at the City of Detroit Receiving Hospital for physicians who have completed training in basic ophthalmology. This large municipal hospital for emergency cases and indigent patients needs additional residents to staff an eight story addition and offers opportunity for clinical and surgical training, as well as research in ophthalmology, with facilities and staff of the Kresge Eye Institute available. Graduate training is offered in optics, biochemistry, ocular pathology, and motility. Tax-free grants are offered until residents are eligible for the city payroll. For information write Dr. Albert D. Ruedemann, Kresge Eye Institute, 690 Mullett St., Detroit 26.

Northern Michigan Rheumatic Fever Center.—The newly created Northern Michigan Rheumatic Fever Diagnostic and Consultation Center opened in January in Little Traverse Hospital at Petoskey. It will serve the five counties of Antrim, Charlevoix, Cheboygan, Emmet, and Otsego. Since its inception by the Michigan State Medical Society, the program has increased from the original pilot control center at Marquette to 30 diagnostic and consultation centers located in 16 well-defined areas of the state. The rheumatic fever control program is operated throughout the state by the medical society as a service to the people. The program receives no government aid. The major portion of its financial support comes from the Michigan Heart Association. Yearly grants are also provided by the Michigan Chapter of the Arthritis and Rheumatism Foundation and the Michigan Society for Crippled Children.

MINNESOTA

The Nineteenth Judd Lecture.—The 19th E. Starr Judd Lecture will be given by Dr. Thomas G. Orr, professor of surgery, University of Kansas, Kansas City, March 20 at 8:15 p. m. in Owre Hall at the University of Minnesota, Minneapolis, on treatment of carcinoma of the pancreas. The late E. Starr Judd, an alumnus of the medical school, established this lectureship in surgery a few years before his death.

MISSOURI

Joint Meeting of Chest Physicians and Trudeau Societies.—The Missouri chapters of the American College of Chest Physicians and the Trudeau Society will meet at the Jefferson Hotel in St. Louis, March 30 beginning at 12 noon. There will be a round-table discussion on valvulotomy under the chairmanship of Dr. David B. Flavan. Dr. Osler A. Abbott of Emory University School of Medicine, Atlanta, will speak on "Cineradiography in the Study of Thoracic Lesions"; Dr. Louis L. Friedman of Birmingham, Ala., will discuss "Antracosis." The meeting will close with a paper by Dr. LeRoy Sante, St. Louis, on "Azotemic Edema of the Lung and Its Relationship to Collagen Disease."

Personals.—Dr. W. Barry Wood Jr., Busch Professor of Medicine at Washington University School of Medicine, St. Louis, served as physician-in-chief pro tempore at the Peter Bent Brigham Hospital in Boston for the week of Jan. 14.—Dr. Robert A. Moore, dean, Washington University School of Medicine, St. Louis, left Feb. 12 for Bangkok, Thailand, where, as director of the Washington University-Thailand medical schools teaching assistance program, he will lecture on pathology and observe results of the exchange program. Washington University School of Medicine became the first school in the nation to establish a cooperative teaching program under the Marshall Plan when plans for the project were completed last April (THE JOURNAL, May 19, 1951, page 265).—Dr. Cecil G. Baker, assistant in neurology and psychiatry, St. Louis University School of Medicine, left on Feb. 25 for Iowa City to become acting chief of the neuropsychiatric service at the new Veterans Administration Hospital, which is expected to be opened the first week in March.

MONTANA

New Community Hospital.—The Murray Hospital, which has been functioning in Butte for over 50 years, closed its doors on Jan. 21, and the patients were transferred to the new Butte Community Memorial Hospital. However, the Murray Clinic, which owned and operated the Murray Hospital, is continuing to operate as a clinic in its building at 9 W. Granite St. The new Butte Community Memorial Hospital is a \$4.5 million institution of 122 beds donated to the community by the Anaconda Copper Mining Company. Dr. William B. Talbot is administrator and chief-of-staff.

NEW YORK

Society of Mental Health.—The New York State Society for Mental Health, succeeding the Committee on Mental Health of the State Charities Aid Association, has been organized as a part of the association to carry out a program of mental health throughout the state. The group, made up of both lay and professional persons, will expand the mental health work the association has been doing for 45 years. One of its first projects will be the creation of a committee to study all New York State laws affecting mental health.

New York City

Columbia Tuition Raised.—Columbia University has raised tuition in its 17 schools and departments effective next fall. The schools of medicine and dentistry will charge \$825 a year in place of the present \$750. The increases are the third in a decade.

The Isidore Friesner Lecture.—Dr. George Gomori, professor of medicine at the University of Chicago, will deliver the Isidore Friesner Lecture of the Mount Sinai Hospital of New York March 7 at 8:30 p. m. in the Blumenthal Auditorium. His subject will be "Histochemistry of Enzymes."

Anniversary Volume Honors Dr. Jaffe.—The October, 1951, *Bulletin of the Hospital for Joint Diseases* is dedicated to Dr. Henry L. Jaffe, pathologist and director of laboratories of the hospital, and commemorates the 25th anniversary of his association with the hospital. The 527 page issue contains essays written by 34 of Dr. Jaffe's medical friends and admirers.

Lecture on Cortisone and Cancer.—Louis F. Fieser, Ph.D., Sheldon Emery Professor of Organic Chemistry at Harvard University, Boston, will speak on "Cortisone and the Cancer Problem" March 20 at 8 p. m. in the Great Hall, City College of New York. The lecture is the fourth in a series of Bicentennial Science Lectures of the City College.

Meeting on Pulmonary Hazards of Industry.—As a part of the annual meeting of the New York Trudeau Society on March 5 the first joint meeting of this group and the Tuberculosis Sanatorium Conference of Metropolitan New York will be held at 8:15 p. m. at Cornell University Medical College amphitheatre. The subject, "Pulmonary Hazards in Industry," will be discussed by Dr. Arthur J. Vorwald, director of research, Trudeau Foundation, Saranac Lake, N. Y., and Dr. Irving Graef, associate professor of clinical medicine, New York University Post-Graduate Medical School. Discussion leaders are Dr. Anthony J. Lanza, also of the Post-Graduate Medical School, and Dr. Leonard Greenburg of the State of New York Department of Labor, New York. The Tuberculosis Sanatorium Conference of Metropolitan New York serves as a forum for the informal consideration of problems and matters of general and local interest in the medical, nursing, and business administration of tuberculosis sanatoriums and hospitals. The conference is supported by the Tuberculosis and Health Associations of Brooklyn, Queens, New York, Yonkers, and of Nassau, Rockland, Suffolk, and Westchester counties.

NORTH CAROLINA

Brevard Sewage Treatment Plant.—Brevard completed improvements on the town's water supply and dedicated and placed in operation its new sewage treatment plant late last year. The plant is the first to be constructed in the French Broad River Basin. Brevard is located in a rapidly developing industrial area. The city made plans to develop its water resources both for industrial and recreational values prior to the passage of the stream sanitation law in 1951 by the general assembly. The total cost of the improvements was about \$500,000.

University Appointments.—Dr. William L. Fleming, professor preventive medicine at Boston University School of Medicine, go to the University of North Carolina later this year. He will be professor of preventive medicine and director of the medical outpatient clinic of the new University Hospital of the medical school at Chapel Hill when it opens. Dr. Fleming from 1939 to 1945 was professor of syphilology at the University of North Carolina. Dr. George C. Ham, who has been at the Institute for Psychoanalysis in Chicago, joined the university in December as professor of psychiatry. Dr. William James Cromartie, associate professor of bacteriology and medicine at the University of Minnesota, Minneapolis, has been appointed associate professor in bacteriology and director of the bacteriological laboratory in the University Hospital.

OHIO

Society News.—The Mahoning County Medical Society celebrated its 80th anniversary at a dinner at the Youngstown Country Club, Jan. 15. The new president, Dr. Carl A. Gustafson, Youngstown, was inaugurated at this meeting.

Diagnosis and Treatment of Malignant Disease.—On April 3-5 the Frank E. Bunts Institute and the Cleveland Clinic Foundation will present a continuation course for physicians on "The Diagnosis and Treatment of Malignant Disease." Dr. Freddy Homburger, research professor of medicine, Tufts College Medical School, Boston, will give the evening lecture April 4. The other guest speakers will be Dr. Allan C. Barnes, professor of obstetrics and gynecology and chairman of the department, Ohio State University College of Medicine, Columbus; Dr. Brown M. Dobyns, associate professor of surgery, Western Reserve University School of Medicine, Cleveland; and Dr. Thomas D. Kinney, director of laboratories, Cleveland City Hospital, and professor of pathology, Western Reserve University School of Medicine. Inquiries may be addressed to the Frank E. Bunts Educational Institute, 2020 East Ninety-third St., Cleveland 6.

OKLAHOMA

Long Memorial Lecture.—Dr. Arthur Grollman, professor of experimental medicine, Southwestern Medical School, Dallas, will deliver the Leroy Long Memorial Lecture at the University of Oklahoma School of Medicine, Oklahoma City, on the evening of March 14.

OREGON

State Board of Health Appointments.—Dr. Otto C. Hagmeier of Seaside has been elected president of the Oregon State Board of Health succeeding Dr. Thomas E. Griffith of The Dalles. Dr. Hagmeier practiced 40 years before his recent retirement. Named to assist him are Dr. Norman E. Irvine, Lebanon, first vice-president, and L. L. Riggs, Portland, second vice-president. Dr. Harold M. Erickson, Portland, will continue as secretary and state health officer.

TENNESSEE

Dr. Quinn to Head Department at Vanderbilt.—Dr. Robert William Quinn, associate professor of preventive medicine University of Wisconsin Medical School, Madison, has been appointed professor and head of the department of preventive medicine and public health at Vanderbilt University School of Medicine, Nashville. Dr. Quinn graduated from McGill University Faculty of Medicine, Montreal, in 1938. After active duty with the U. S. Navy (MC) Reserve, 1942-1946, he became research fellow in preventive medicine at Yale University School of Medicine and then instructor in preventive medicine there. He has been at the University of Wisconsin Medical School since 1949. Dr. Quinn will assume his duties at Vanderbilt in June, 1952, and Dr. Alvin E. Keller, who has been acting head of the department at Vanderbilt, will continue as associate professor of preventive medicine and public health.

TEXAS

Southwestern Medical School Buildings.—At its meeting on Feb. 1-2, the board of regents of the University of Texas approved preliminary plans for a \$2,750,000 basic science building for Southwestern Medical School in Dallas. It is expected that this building, the first unit on the school's permanent campus may be completed by the summer of 1953. A request for funds for a clinical building will be presented to the next state legislature.

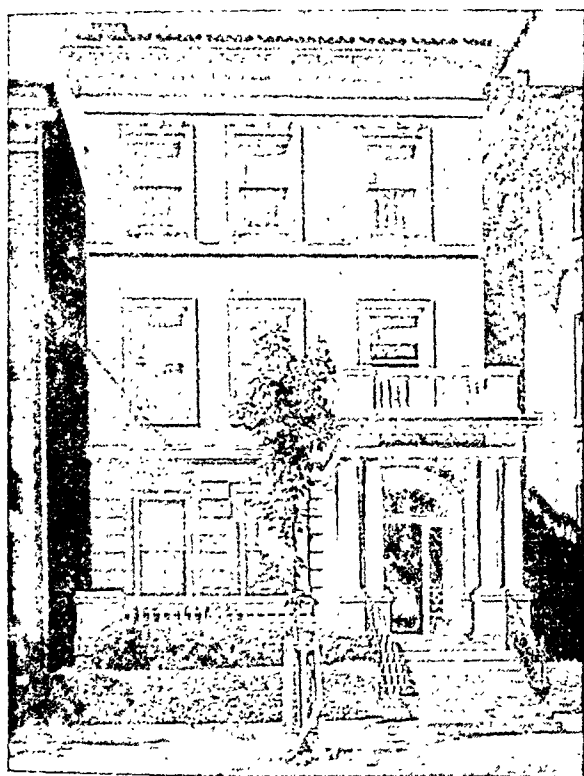
Meetings on Tumors.—Several meetings will be held at the Texas Medical Center, Houston, on April 25-26. At the Sixth Annual Symposium on Fundamental Cancer Research of the University of Texas M. D. Anderson Hospital for Cancer Research, a half-day will be devoted to papers on nutritional factors in cancer. The Cancer Pathology and Radiology Conference of The University of Texas M. D. Anderson Hospital and Postgraduate School of Medicine will be on tumors and other diseases of bone. The South Central Section of the College of American Pathologists will participate. Dr. Maxwell M. Witrobs, professor of medicine, University of Utah, Salt Lake City, is arranging the session on nutritional factors in cancer. Dr. Granville A. Bennett, professor of pathology, University of Illinois, Chicago, and Dr. L. Henry Garland, clinical professor of radiology, Stanford University Medical School, San Francisco, will jointly conduct the Conference on Tumors and Other Diseases of Bone. The third Bertner Foundation Lecture and Award will be made at the banquet on April 25. Information may be obtained from Dr. William O. Russell, 2310 Baldwin St. Houston 6.

VIRGINIA

Gill Memorial Hospital Congress.—The 25th annual spring congress of the Gill Memorial Eye, Ear and Throat Hospital will be held April 7-12 in Roanoke. The program will include lectures and demonstrations of interest to eye, ear, and throat specialists. The fee is \$75. The faculty includes Drs. Francis H. Adler, Philadelphia; James H. Allen, New Orleans; Hermann M. Burian, Iowa City; W. Edward Chamberlain, Philadelphia; Paul J. Chandler, Boston; Kenneth M. Day, Pittsburgh; John H. Du

nington, New York; Edwin B. Dunphy, Boston; Frederick A. Figi, Rochester, Minn.; Watson Gailey, Bloomington, Ill.; Leslie N. Gay, Baltimore; Henry M. Goodyear, Cincinnati; Bayard T. Horton, Rochester, Minn.; Robert M. Hosler, Cleveland; Howard P. House, Los Angeles; Chevalier L. Jackson, Philadelphia; Edward C. Kendall, Ph.D., Princeton, N. J.; T. Keith Lyle, London, England; Surgeon General H. Lamont Pugh, USN, Washington, D. C.; Hunter H. Romaine, New York; Frank B. Walsh, Baltimore, and James C. White, Boston. There will also be special guests representing national medical organizations at this silver anniversary of the congress.

New State Society Headquarters.—The headquarters of the Medical Society of Virginia has been moved to 1105 W. Franklin St., Richmond. The building, purchased about a year ago at a cost of \$26,500, is a 13 room house built over 40 years ago. The first floor accommodates the joint activities of the society and the *Virginia Medical Monthly*. The front room on the second floor has been rented to the Virginia Academy of General



New headquarters for the Medical Society of Virginia.

Practice, and it is anticipated that other rooms will be rented. The society formerly had its headquarters in the Richmond Academy of Medicine building.

WISCONSIN

Marquette Spring Clinics.—The Alumni Association of Marquette University School of Medicine will hold its spring clinics at the medical school in Milwaukee, March 29. Chairmen of the program are Drs. Robert D. O'Connor, Leo R. Weinshel, and George E. Collentine Jr. There will be an informal dinner dance at the Wisconsin Club.

Dr. Frost Honored.—After 43 years of service on the board of directors of Morningside Sanatorium in Madison, William D. Frost, Ph.D., emeritus professor of bacteriology, University of Wisconsin, has retired as president of this organization. Dr. Frost, who is 84, was honored at a testimonial dinner at the University Club, Feb. 29. Since its founding in 1917, Morningside has expanded its facilities from 10½ to 30 acres and a half dozen modernly equipped buildings. In addition to administrative duties, Dr. Frost has maintained interest in every patient, done all the x-ray work, supervised the laboratory, and helped develop the children's center.

GENERAL

Grant to Aid Pediatric Education.—The National Foundation for Infantile Paralysis has made a grant of \$10,000 to the American Academy of Pediatrics to be used by the Committee on Medical Education to improve pediatric education. This grant will enable the Medical Education Committee to hold 10 regional conferences on pediatric education in 1952.

New Medical Journal.—The first issue of *Metabolism*, bimonthly journal devoted to clinical and experimental metabolism, appeared in January. Drs. Samuel Soskin, Chicago, and Fuller Albright, Boston, the editors, are assisted by a board of associate editors and corresponding editors from 14 countries. The journal is designed to present to the clinician the practical applications of recent advances in metabolism. It will also attempt to keep the research worker abreast of clinical problems.

Research in Human Fertility.—The Planned Parenthood Federation of America is offering grants for basic research relating to problems of human fertility, including infertility and conception. The grants are being made available through the federation's Robert L. Dickinson Research Memorial. Applications will be received and screened by a subcommittee of the medical committee of the federation. Applicants should address the Robert L. Dickinson Research Memorial, Planned Parenthood Federation of America, 501 Madison Ave., New York 22.

Society Elections.—At the annual meeting of the American College of Radiology in Chicago, Feb. 8, the following officers were elected: Dr. John S. Bouslog, Denver, president; Dr. Robert P. Ball, Baton Rouge, La., vice-president; Dr. John D. Camp, Los Angeles, chairman of the board of chancellors, and Dr. Earl E. Barth, Chicago, treasurer. At the annual banquet the Gold Medal of the American College of Radiology was awarded to Dr. George E. Pfahler of Philadelphia for "distinguished and extraordinary service to the college and to the profession for which it stands." This was the eighth such medal awarded in the 30-year history of the college. Dr. Pfahler, the first president of the American College of Radiology, also has served as president of the American Roentgen Ray Society and the American Radium Society.

Railway Surgeons Association.—The annual meeting of the American Association of Railway Surgeons will be held at the Drake Hotel, Chicago, April 1-3, under the presidency of Dr. D. Ray Murdock, Greensburg, Pa. In addition to 16 papers to be presented at the meeting, there will be a symposium on vascular disorders on Wednesday evening with the following speakers:

- Martin H. Wendkos, Philadelphia, Outlook for the Railroad Employee with Heart Disease.
- Eric Oldberg and Oscar Sugar, Chicago, Diagnosis and Treatment of Cerebral Vascular Lesions.
- Leo M. Zimmerman, Chicago, Thrombosis and Embolism.
- Walter W. Carroll, Chicago, Trends in Treatment of Varicose Veins.

At the dinner Wednesday evening the Honorable Walter H. Judd, M.D., Congress of the United States, 5th District, Minnesota, will speak on "Which Way America?"

New Journal on Diabetes.—The first issue of *Diabetes, The Journal of the American Diabetes Association*, a bimonthly publication, appeared in February. It will be the association's official scientific and organizational publication, replacing its annual *Proceedings* and its quarterly *Diabetes Abstracts*, both of which have been published for 10 years. *Diabetes* is being edited by Dr. Frank N. Allan of the Lahey Clinic, Boston, first vice-president of the American Diabetes Association, who will be assisted by a 16-member editorial board under the chairmanship of Dr. Charles H. Best of the University of Toronto, Canada. There are also four consulting foreign editors. The first issue contains eight scientific papers, abstracts, editorials, an historical biography, diabetes statistics, book reviews, and an organization section. The subscription rate is \$9 a year for nonmembers of the association; members will receive it without charge. The editorial offices are at 11 West 42nd St., New York 18.

American Congress in Obstetrics and Gynecology.—The Fifth American Congress on Obstetrics and Gynecology will be held in Cincinnati's Netherland-Plaza Hotel March 31 through April 4. It is sponsored by the American Committee on M-

fare. In addition to a comprehensive medical program, there will be papers on nursing and public health and a special session on sociologic factors. The latest developments on proposed legislation for emergency medical and infant care will be presented by Dr. Joseph Lawrence, director of the American Medical Association's Washington office. There also will be discussions on education for the patient, the doctor, the student, and the hospital. Techniques, conclusions, and follow-up action in Chicago's recent investigation of neonatal deaths of 10,000 infants will be revealed in a symposium on the public health program, under the chairmanship of Dr. Herman N. Bundesen, president of the Chicago Board of Health. The scientific and clinical program will cover all aspects of obstetrics and gynecology. Among the subjects will be sterility, fetal wastage, Rh and Hr sensitization, and uterine carcinoma. Among the speakers will be Dr. Woodard D. Beacham, New Orleans, medical section chairman, and Dr. Nicholson J. Eastman, Baltimore, general program chairman. Among the special exhibits will be a demonstration of prenatal exercises by the Maternity Center Association, a typical home delivery by the Frontier Nursing Service of Kentucky, a display of cytology smears prepared by Duke University and employing more than 100 microscopes, and a demonstration of nurse anesthesia by the American Association of Nurse Anesthetists.

Airline Medical Directors Association.—The annual meeting of this association was held Feb. 22-23 at the Randolph Field headquarters of the Air Force School of Aviation Medicine in Texas in order to study the research work being done by the Air Force on medical problems of flight. Members of the association, an international organization representing the medical services of the world's major airlines, toured the air force base and visited the research laboratories at the school. Among the questions discussed were sudden deceleration and crash prevention, prevention of epidemics arising from worldwide air travel, toxic materials such as fuels used in highspeed aircraft, and the problem of aging. Several foreign medical advisers attended the meeting. Dr. Francis N. Kimball of New York is president of the association, and Dr. Percy B. Wiltberger, Columbus, Ohio, the retiring president.

American Psychosomatic Society.—This society will hold its annual meeting March 29-30 at the Drake Hotel, Chicago, under the presidency of Dr. Roy R. Grinker, Chicago. In addition to papers to be presented, there will be discussions as follows:

Psychophysiological Changes After Thalamotomy, H. Keith Fischer, Herbert Freed, Carlton Orchinik, M.A., Philadelphia.

Observations on Psychodynamic Changes in Patients Receiving Artificial Insemination, Fred P. Robbins and Therese F. Benedek, Chicago, George C. Ham, Chapel Hill, N. C.

Effect of Psychoanalysis on the Course of Peptic Ulcer: A Preliminary Report, Leonard A. Stine, Andrew C. Ivy, Chicago.

Emotions and HCl Secretion During Psychoanalytic Hours, George F. Mahl, Ph.D., Richard Karpe, New Haven, Conn.

Psychodynamics of Peptic Ulcer Pathogenesis in Hospitalized Schizophrenic Patients, Melvin Myron Katz, Ph.D., Northport, N. Y.

An Experimental Investigation in Anxiety: Interdisciplinary Research in Life Situations, Sheldon J. Korchin, Ph.D., Harold Persky, Ph.D., Harold Basowitz, Ph.D., and Dr. Grinker.

A Preliminary Report on the Emotional Aspects of the Respirator Care of Patients with Poliomyelitis, Dane G. Prugh and Consuelo K. Tagiuri, Boston.

Psychogenic Factors and Psychotherapy in Raynaud's Syndrome, John A. P. Millet and Bela Mittelman, New York, and Harold I. Lief, New Orleans.

Further Observations on Psychological Factors in Patients with Lymphomas and Leukemias, William A. Greene Jr., Rochester, N. Y.

WHO Executive Board Meeting.—The Executive Board of the World Health Organization ended its ninth session at Geneva Feb. 4 under the chairmanship of Dr. Jacques Parisot, (France). The board appointed Dr. Parisot, Dr. A. L. Bravo (Chile) and Dr. W. A. Karunaratne (Ceylon) as its official representatives to the next or Fifth World Health Assembly, to meet May 5-25 in Geneva. Among other recommendations to the assembly was a larger budget for 1953. The board recommended the inclusion of Algeria, Greenland, Morocco, and Tunisia in the European region, and the inclusion of the trust territory of Somaliland under Italian administration in the Eastern Mediterranean Region. Dr. Norman D. Begg of Scotland and Dr. Francois Daubenton of the Netherlands were selected as directors of the WHO

regional offices for Europe and Africa, respectively. Dr. Pierre Montus, director of the child health department of Paris is the new deputy director of the European Regional Office. The board also confirmed the choice of Geneva as the temporary location for the Regional Office for Europe and of Brazzaville as the seat of the Regional Office for Africa. Two long-range programs evolved by the World Health Organization with other United Nations Agencies were approved. The international program for children, designed to assist governments in a variety of fields, lays down principles for child welfare programs as integral parts of national health services, and gives high priority to a joint program to aid governments in training community auxiliary workers in health, social welfare, and nutrition in underdeveloped areas. It is proposed to establish a limited number of such pilot training projects in 1952. The international plan for rehabilitation of physically handicapped persons is designed to serve as a guide to countries at various stages of economic development. It includes recommendations for the promulgation of measures to prevent or limit physical disability, for awakening of public opinion concerning the handicapped, and for the development of rehabilitation methods for the reconditioning, training, and employment of all classes of handicapped persons.

Central Surgical Association.—The annual assembly of the Central Surgical Association will be held in Toronto, Canada, at the Royal York Hotel, March 7-8, under the presidency of Dr. B. Noland Carter, Cincinnati. An invitation clinic day will be held March 6 at the Toronto General Hospital and Hospital for Sick Children. Physicians delivering papers by invitation include:

Elden C. Weckesser, John F. Lindsay Jr., Frank A. Cebul, Cleveland, Plication of Small Intestine for Obstruction Due to Adhesions.

Jack H. Hertzler, Birmingham, Mich., Experimental Method for Everting End-to-End Anastomosis in Gastrointestinal Tract.

Frank J. Rack, James R. Mincks, Fiorindo A. Simeone, Cleveland, Etiology of Esophageal Varices.

Robert H. Clifford, Detroit, Evaluation of Three Methods of Treatment for Finger Tip Amputation.

Merle M. Musselman, Eloise, Mich., Wayne W. Glas, Ann Arbor, Mich., and Thomas D. Grekin, Detroit, U. S. Army Medical Corps, Fat Embolism: Clinical Investigation.

Gould A. Andrews, Oak Ridge, Tenn., Intracavitary Colloidal Radioactive Gold in Treatment of Effusions Caused by Neoplasms.

William Cox, Indianapolis, Impedance Plethysmography in Study of Peripheral Circulatory Disorders.

F. John Lewis, Milton P. Reiser, Richard H. Egdahl, Minneapolis, Clinical Uses of Artificial Kidney.

The dinner dance will be Friday evening. The guest speaker will be Dr. Hans Selye, professor of experimental medicine and surgery at the University of Montreal Faculty of Medicine, on "Recent Advances in the General-Adaptation-Syndrome."

Surgeons Sectional Meeting in Minneapolis.—A sectional meeting of the American College of Surgeons will be held at the Radisson Hotel, Minneapolis, March 24-26. In addition to separate papers, the scientific program includes the following panel discussions and symposiums:

Breast Tumors, Orwood J. Campbell, Minneapolis, moderator, with Anthony R. Curreri, Madison, Wis., and Paul W. Schafer, Kansas City, Kas.

Intestinal Obstruction, Owen H. Wangenstein, Minneapolis, moderator, with Carl W. Eberbach, Milwaukee, Frederick C. Hill, Omaha, and Lloyd F. Sherman, Minneapolis.

Symposium on Trauma, Dr. Schafer and Daniel J. Moos and Richard S. Rodgers, Minneapolis.

Symposium on Cancer, T. Brannon Hubbard, Minneapolis, Wallace P. Ritchie, St. Paul, and John B. Erich, Rochester, Minn.

Hysterectomy: Total, Subtotal, or Vaginal, John W. Huffman, Chicago, moderator, with Paul N. Larson, Minneapolis, Joseph H. Pratt, Rochester, Minn., and Charles G. Uhley, Crookston, Minn.

Bleeding from Gastrointestinal Tract, Charles E. Rea, St. Paul, moderator, with Thomas C. Douglass, Chicago, and Lyle J. Hay and J. John Lewis, Minneapolis.

At the dinner meeting on Monday, J. O. Christianson, D.Sc., Minneapolis, will speak on "Rediscovering America," and Dr. Paul R. Hawley, Chicago, director, American College of Surgeons, will speak on "Your College: What It Means to You and to Me." The Minneapolis Surgical Society will hold its 30th anniversary banquet at 6:30 p. m. Tuesday. Dr. George Crile Jr. of the Cleveland Clinic Foundation will speak on "Recent Trends in Thyroid Surgery." The Minnesota Academy of Ophthalmology and Otolaryngology will present a program on otolaryngology in conjunction with the American College of Surgeons on Tuesday.

CANADA

Glaucoma Laboratory.—The University of Toronto has established a glaucoma laboratory in the Banting Institute to be directed by Dr. Thomas H. Hodgson. The laboratory will undertake basic studies in conjunction with the glaucoma clinic service. A grant from the Ontario Provincial Department of Health made the laboratory possible.

LATIN AMERICA

Society News.—The Cuban Society of Dermatology and Syphilography has elected the following officers for 1952: Dr. Jose de Castro Palomino, president; Dr. Fernando Trespalacios, vice-president; Dr. Guillermo Gonzalez Peris, secretary, and Dr. Pastor Farinas, treasurer.

Meetings on Gastroenterology in Mexico.—The third Pan-American Medical Week of Gastroenterology and the First National Congress of Gastroenterology will take place in Mexico City May 11-17. The meetings will be held under the auspices of the Inter-American and Mexican Associations of Gastroenterology. The main topic will be the pancreas, and papers will deal with surgical, medical, biochemical, diagnostic, and physiologic problems. The secretary general is Dr. R. Flores-Lopez, Cientifica del Hospital General, Mexico, 9, D. F.

FOREIGN

WHO-Aided Malaria Campaign in Philippines.—The first Philippine malaria control project to be aided by the World Health Organization began Feb. 16 on the island of Mindoro. Since most residents of Mindoro are rice farmers, the program to control the disease is expected to result in great improvement in food production. The team will endeavor to protect more than 50,000 persons against malaria. Following this WHO-assisted phase, Philippine government control teams will take over and extend control measures. The method to be used is residual spraying of dichlorodiphenyltrichloroethane (DDT) and BHC. Transport of insecticides and sprayers will be provided by the government. WHO is supplying international experts, laboratory equipment and supplies, technical literature, and additional transport.

Ramon y Cajal Prize Awarded.—The Ramon y Cajal Prize, given by the Spanish Government, has been awarded Dr. Jose Manuel Rodriguez Delgado, research fellow in physiology at Yale University School of Medicine, New Haven, Conn., for his paper on a new technique whereby he implants electrodes in the brains of laboratory animals to study the functions of the brain. The prize, which carries an honorarium of about \$1,000, was established by Spain in honor of the late Dr. Santiago Ramon y Cajal, co-winner in 1906 of the Nobel Prize for his work on the structure of the nervous system. Dr. Delgado, a native of Rondo, Spain, received his medical training at the University of Madrid and has been on the faculty there since receiving his medical degree. He also is a member of the Cajal Research Institute, which is associated with the university.

Medical Mission to East Asia.—A World Health Organization team of eleven medical scientists from seven countries will shortly visit Burma, Ceylon, and India to work with medical-education projects similar to those carried out last year in the Middle East. The visits will have three main purposes: exchange of information with local medical specialists, lectures and demonstrations on advances in medical techniques, and discussion of problems relating to medical education in the host countries. The visiting scientists will advise in their special fields if such advice is expressly sought by host governments. The team is under the chairmanship of Dr. Erik Husfeldt, professor of thoracic surgery at the University of Copenhagen. It was scheduled to arrive in Calcutta on February 4, in Rangoon on February 13, and in Colombo early in March. The team will include the following specialists: Dr. Erik Wain Anderson, anesthesia, Copenhagen; Dr. E. W. H. Cruikshank, physiology, Aberdeen, Scotland; Dr. Marcel Florin, biochemistry, Liège, Belgium; Dr. John E. Gordon, epidemiology, Boston; Dr. Edward Grzegorzewski, public health, Geneva, Switzerland; Dr. Erik Husfeldt, thoracic surgery, Copenhagen; Dr. Malcolm R.

MacCharles, surgery, Winnipeg, Manitoba, Canada; Dr. H. O. Schild, pharmacology, London; Dr. B. Vahlquist, pediatrics, Uppsala, Sweden; Dr. F. S. P. Van Buchem, medicine, Groningen, Holland, and Dr. Rohan Williams, radiology, London.

Tuberculosis Training Center in New Delhi.—A tuberculosis training center will be opened in New Delhi early in 1952. It represents an extension of the Tuberculosis Association of India's existing clinic in the Irwin Hospital Compound. Both centers will continue to be under the direction of Dr. B. K. Sikand. X-ray and laboratory equipment, provided by the United Nations International Children's Emergency Fund, has been installed. WHO has also provided an international team consisting of a bacteriologist, an epidemiologist, a laboratory and x-ray expert, and a public health nurse to work, during the first years of the center's operation, with a similar local team provided by the Tuberculosis Association of India.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Part II*, April 21-22; *Parts I and II*, June 16-18 or June 23-25; *Part I*, September. All centers where there are five or more candidates. Exec. Sec., Dr. John P. Hubbard, 225 S. 15th St., Philadelphia 2.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: Various Locations, July 18. Final date for filing application was Jan. 18. Sec., Dr. C. B. Hickcox, 80 Seymour St., Hartford 15.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written*. Various centers. March 1952. *Oral*. Chicago, May 1952. Final date for filing application was Feb. 1, 1952. Candidates for these tests must have completed three years of approved training prior to July 1, 1952. Sec., Dr. George M. Lewis, 66 E. 66th St., New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written*. Various centers and overseas, Oct. 20. Closing date for the acceptance of applications for the written examination will be May 1. *Oral*. Cleveland, April 17-19; Chicago, June 5-7, San Francisco, September or October; New York City, November or December. Exec. Sec.-Treas., Dr. William A. Werrell, 1 West Main Street, Madison 3.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral*. Chicago, May 1952. Final date for filing applications for the May 1952 examination was Jan. 1. Sec., Dr. W. J. German, 789 Howard Ave., New Haven 4, Conn.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Oral*. Chicago, June 9-13, 1952. Final date for filing application was Feb. 1, 1952. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Practical*. Philadelphia, May 29-June 3; Chicago, Oct. 6-10 and New York City, June 6-10, 1953. Sec., Dr. Edwin B. Dunphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral*. Toronto, May 13-17; Chicago, Oct. 6-10. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PEDIATRICS: *Oral*. St. Louis, Mo., Mar. 21-23; Washington, D. C., May 3-5; San Francisco, late June; Chicago, October and Boston, late November. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION: *Parts I and II*. Chicago. June 8 and 9. Sec., Dr. Robert L. Bennett, Georgia Warm Springs Foundation, Warm Springs, Ga.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral and Written*. St. Louis, May 17-19. Sec., Dr. Bradford Cannon, 4647 Pershing Ave., St. Louis 8.

AMERICAN BOARD OF PREVENTIVE MEDICINE AND PUBLIC HEALTH. *Written*. Berkeley, Calif., Minneapolis, New Orleans and Baltimore. April 18. Sec., Dr. Ernest L. Stebbins, 615 N. Wolfe St., Baltimore.

AMERICAN BOARD OF PROCTOLOGY. *Part I*. Kansas City, Minneapolis, Philadelphia and San Francisco. May 3. Examination includes both oral and written examinations in the basic sciences. *Dates and places tentative*. Sec., Dr. Louis A. Buie, 102-110 2d Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: Chicago, June 13-14. Final date for filing applications is March 15. New York City, Dec. 15-16. Final date for filing applications is Sept. 15. Sec.-Treas., Dr. David A. Boyd, Jr., 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Oral*. Spring 1952. Final date for filing application was Dec. 31. Sec., Dr. B. R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written*. Various Centers. March 1952. Final date for filing application was Dec. 1, 1951. The following written examination will be given in October 1952. Sec., Dr. J. Stewart Rodman, 225 S. 15th St., Philadelphia.

BOARD OF THORACIC SURGERY: Various parts of the country. *Written*. Feb. 29, 1952. Final date for filing application is Jan. 15. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2.

MEETINGS

AERO MEDICAL ASSOCIATION, Washington, D. C., March 17-19. Dr. Thomas H. Sutherland, 214 South State St., Marion, Ohio, Secretary.

ALABAMA, MEDICAL ASSOCIATION OF THE STATE OF, Montgomery, April 17-19. Dr. Douglas L. Cannon, 519 Dexter Ave., Montgomery, Secretary.

AMERICAN ACADEMY OF FORENSIC SCIENCES, Biltmore Hotel, Atlanta, Ga., March 6-8. Prof. Ralph F. Turner, Michigan State College Dept. of Police Administration, East Lansing, Mich., Secretary.

AMERICAN ACADEMY OF GENERAL PRACTICE, Atlantic City, N. J., March 24-27. Mr. Mac F. Cahal, 406 West 34th St., Kansas City 2, Mo., Executive Secretary.

AMERICAN ACADEMY OF OBSTETRICS AND GYNECOLOGY, Cincinnati, April 1. Dr. Ralph A. Reis, 116 South Michigan Boulevard, Chicago 3, Secretary.

AMERICAN ASSOCIATION OF ANATOMISTS, Providence, R. I., March 19-21. Dr. Normand L. Hoerr, 2109 Adelbert Road, Cleveland 6, Secretary.

AMERICAN ASSOCIATION OF IMMUNOLOGISTS, New York, April 14. Dr. John Y. Sugg, 1300 York Ave., New York, Secretary.

AMERICAN ASSOCIATION OF PATHOLOGISTS AND BACTERIOLOGISTS, New York, April 10-12. Dr. Alan R. Moritz, 2085 Adelbert Road, Cleveland 6, Secretary.

AMERICAN ASSOCIATION OF RAILWAY SURGEONS, Drake Hotel, Chicago, April 1-3. Dr. Chester C. Guy, 5800 Stony Island Ave., Chicago 37, Secretary.

AMERICAN COLLEGE OF ALLERGISTS, William Penn Hotel, Pittsburgh, April 7-9. Dr. Fred W. Wittich, 423 LaSalle Medical Bldg., Minneapolis 2, Secretary.

AMERICAN COLLEGE OF SURGEONS, SECTIONAL MEETINGS:
 Minneapolis, Radisson Hotel, March 24-26. Dr. Harvey Nelson, 78 South 9th St., Minneapolis 2, Chairman.
 Tucson, Ariz., Pioneer Hotel, April 7-9. Dr. Meade Clyne, 110 South Scott St., Tucson, Chairman.
 Vancouver, B. C., Vancouver Hotel, March 31-April 4. Dr. J. Russell Neilson, 925 West Georgia St., Vancouver, B. C., Chairman.

AMERICAN CONGRESS ON OBSTETRICS AND GYNECOLOGY, Netherlands-Plaza Hotel, Cincinnati, March 31-April 4. Dr. Luella E. Nadelhoffer, 116 South Michigan Ave., Chicago 3, Secretary.

AMERICAN DERMATOLOGICAL ASSOCIATION, Broadmoor Hotel, Colorado Springs, Colo., Apr. 23-26. Dr. Louis A. Brunsting, 102 Second Ave. S.W., Rochester, Minn., Secretary.

AMERICAN HEART ASSOCIATION, Hotel Statler, Cleveland, April 17-20. Dr. William H. Bunn, 1775 Broadway, New York 19, Secretary.

AMERICAN PSYCHOSOMATIC SOCIETY, Chicago, March 29-30. Dr. Frederick C. Redlich, 551 Madison Avenue, New York 22, Secretary.

AN SOCIETY FOR EXPERIMENTAL PATHOLOGY, New York, April 14-18. Russell L. Holman, 1542 Tulane Ave., New Orleans 12, Secretary.

AN SOCIETY FOR PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, Hotel Statler, New York, April 14-18. Dr. Carl C. Pfeiffer, 1835 W. Polk St., Chicago 12, Secretary.

AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, New York, April 14-18. Dr. Elmer H. Stoltz, 260 Crittenden Blvd., Rochester, N. Y., Secretary.

AMERICAN SURGICAL ASSOCIATION, White Sulphur Springs, W. Va., Apr. 16-18. Dr. Nathan A. Womack, University Hospitals, Iowa City, Secretary.

ARKANSAS MEDICAL SOCIETY, Little Rock, April 21-23. Dr. William R. Brooksher, 215 Kelley Bldg., Fort Smith, Secretary.

CENTRAL SURGICAL ASSOCIATION, Toronto, Can., March 6-8. Dr. James T. Priestley, 102 Second Avenue S.W., Rochester, Minn., Secretary.

CHICAGO MEDICAL SOCIETY ANNUAL CLINICAL CONFERENCE, Palmer House, Chicago, March 4-7. Dr. Walter C. Bornemeier, 86 East Randolph St., Chicago 1, Secretary.

JOHN A. ANDREW CLINICAL SOCIETY, Memorial Hospital, Tuskegee Institute, Ala., April 6-12. Dr. Eugene H. Dibble Jr., Memorial Hospital, Tuskegee Institute, Secretary.

MICHIGAN CLINICAL INSTITUTE, Book-Cadillac Hotel, Detroit, March 12-14. Dr. E. F. Sladek, 606 Townsend St., Lansing 15, Chairman.

MID-CONTINENT PSYCHIATRIC ASSOCIATION, President Hotel, Kansas City, Mo., April 26-27. Dr. Paul Hines, 2625 W. Paseo, Kansas City, Mo., Secretary.

MISSOURI STATE MEDICAL ASSOCIATION, Hotel Jefferson, St. Louis, March 30-April 2. Dr. H. E. Petersen, 634 North Grand Blvd., St. Louis 3, Secretary.

NATIONAL CANCER CONFERENCE, Netherlands Plaza Hotel, Cincinnati, March 3-5. Dr. Charles S. Cameron, 47 Beaver Street, New York, Medical Director.

NEW ORLEANS GRADUATE MEDICAL ASSEMBLY, Municipal Auditorium, New Orleans, March 10-13. Dr. Woodward D. Beacham, 1430 Tulane Ave., Room 105, New Orleans 12, Secretary.

NORTH PACIFIC PEDIATRIC SOCIETY, Portland, Ore., March 8. Dr. Sydney G. Babson, 1020 S.W. Taylor St., Portland 5, Ore., Secretary.

NORTH PACIFIC SOCIETY OF INTERNAL MEDICINE, Portland, Ore., March 22. Dr. R. L. King, 1115 Terry Ave., Seattle 1, Secretary.

PILDMONT PROCTOLOGIC SOCIETY, Charlotte, N. C., March 29-30. Dr. B. Richard Jackson, 224 Hillsboro St., Raleigh, N. C., Secretary.

POST GRADUATE INSTITUTE OF THE PHILADELPHIA COUNTY MEDICAL SOCIETY, Bellevue-Stratford Hotel, Philadelphia, April 1-4. Dr. Thomas M. Durant, 301 South 21st St., Philadelphia 3, Director.

SOUTHEASTERN ALLERGY ASSOCIATION, Bon Air Hotel, Augusta, Ga., March 21-22. Dr. Katharine B. MacInnis, 1515 Bull St., Columbia 49, S. C., Secretary.

SOUTHEASTERN SECTION, AMERICAN UROLOGICAL ASSOCIATION, Boca Raton, Fla., April 2-5. Dr. Russell B. Carson, Sweet Bldg., Fort Lauderdale, Fla., Secretary.

SOUTHEASTERN SURGICAL CONGRESS, Atlanta, Ga., March 10-13. Dr. Benjamin J. Beasley, 701 Hurt Bldg., Atlanta 3, Ga., Secretary.

SOUTHWEST ALLERGY FORUM, Hotel Baker, Dallas, Texas, March 2-4. Dr. James Holman, Medical Arts Bldg., Dallas, Secretary.

TENNESSEE STATE MEDICAL ASSOCIATION, Andrew Johnson Hotel, Knoxville, April 7-9. Mr. V. O. Foster, 504 Doctors Bldg., Nashville 3, Executive Secretary.

UNITED STATES-MEXICO BORDER PUBLIC HEALTH ASSOCIATION, Monterrey, Nuevo Leon, Mexico, March 17-19. Dr. J. C. Ellington, 314 U. S. Court House, El Paso, Texas, Secretary.

WESTERN SOCIETY OF ELECTRO-ENCEPHALOGRAPHY, Del Monte Lodge, Pebble Beach, Calif., March 2-3. Dr. Nicholas A. Bercel, 450 North Bedford Drive, Beverly Hills, Calif., Secretary.

INTERNATIONAL

AUSTRALASIAN MEDICAL CONGRESS, Melbourne Victoria, Australia, Aug. 22-30. Dr. C. H. Dickson, Medical Society Hall, 426 Albert St., East Melbourne, Victoria, Australia, Hon. General Secretary.

COMMONWEALTH AND EMPIRE HEALTH AND TUBERCULOSIS CONFERENCE, Central Hall, London, England, July 8-13. Dr. J. H. Harley Williams, Tavistock House North, Tavistock Sq., London, W.C.1, England, Secretary General.

CONGRESS OF THE INTERNATIONAL DIABETES FEDERATION, Leyden, Netherlands, July 7-12. Dr. F. Gerritzen, 33. Prinsegracht, The Hague, Netherlands, Secretary.

EUROPEAN CONGRESS OF CARDIOLOGY, University of London, Bloomsbury, W.C.1, England, Sept. 10-12. Dr. K. Shirley Smith, 35 Wimpole St., London, W.1, England, Secretary.

EUROPEAN SOCIETY OF CARDIOVASCULAR SURGERY, Strasbourg, France, Oct. 3-4. Sir James Learmonth, Department of Surgery, University New Buildings, Edinburgh 8, Scotland.

INTER-AMERICAN CARDIOLOGICAL CONGRESS, Buenos Aires, Argentina, Aug. 31-Sept. 7. Dr. Blas Moia, Larrea 1132, Buenos Aires, Argentina, Secretary-General.

INTER-AMERICAN CONGRESS OF PUBLIC HEALTH, Havana, Cuba, Sept. 27-Oct. 1. Pan-American Sanitary Bureau, 2001 Connecticut Ave., Washington, D. C.

INTER-AMERICAN CONGRESS OF RADIOLOGY, Mexico City, Mexico, Nov. 2-6. Dr. Guido Torres Martinez, Marsella No. 11, Mexico, D.F., Secretary-General.

INTERNATIONAL COLLEGE OF SURGEONS, Madrid, Spain, May 20-24. Dr. Max Thorek, 850 West Irving Park Road, Chicago, Ill., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF COMPARATIVE PATHOLOGY, Madrid, Spain, May 4-11. Prof. Carda-Aparici, Calle Fernando VI.8, Madrid, Spain, Secretary.

INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY, London, England, July 21-26. Dr. Gordon B. Mitchell-Heggs, 5, Lisle St., London, W.C.2, England, General Secretary.

INTERNATIONAL CONGRESS ON DIABETES, Leyden, The Netherlands, July 7-12. Dr. F. Gerritzen, 33, Prinsegracht, The Hague, Netherlands.

INTERNATIONAL CONGRESS OF HAEMATOLOGY, Mar del Plata, Argentina, Sept. 21-26. Dr. Carlos Reussi, Anchorena 1710, Buenos Aires, Argentina, Secretary.

INTERNATIONAL CONGRESS OF HEALTH TECHNICIANS, Palais de la Mutualite, Paris, France, June 9-14. Secretariat General, 6 Square Desaix, Paris XV^e, France.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Friends House, London, N.W.1, Eng. Sept. 15-18. Sir Harold Boldero, 12 Pall Mall East, London, S.W.1, England, Secretary.

INTERNATIONAL CONGRESS OF LEGAL AND SOCIAL MEDICINE, Berne, Switzerland, April 15-18. Prof. J. Dettling, 20, Buhlstrasse, Berne, Switzerland.

INTERNATIONAL CONGRESS ON MEDICAL RECORDS, London, England, Sept. 7-12. Miss Gwen Perkins, 120 C Street S.E., Washington, D. C., Chairman.

INTERNATIONAL CONGRESS ON NEUROPATHOLOGY, Rome, Italy, Sept. 8-13. Dr. Armando Ferraro, 722 W. 168th St., New York, N. Y., U. S. A., Secretary General.

INTERNATIONAL CONGRESS OF OTO-NEURO-OPHTHALMOLOGY, Lisbon and Estoril, Portugal, April 22-26. Prof. Diogo Furtado, Servico de Neurologia, Hospital dos Capuchos, Lisbon, Portugal, General Secretary.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE, London, England, July 14-19. Dr. A. C. Boyle, 45, Lincoln's Inn Fields, London, W.C.2, England, Hon. Secretary.

INTERNATIONAL CONGRESS FOR THERMALISM AND CLIMATOTHALASSOTHERAPY, Nice-Cannes, France, April 3-8.

INTERNATIONAL SOCIETY OF GEOGRAPHIC PATHOLOGY, Liège, Belgium, July 15-18. Dr. Fred C. Roulet, Habelstr. 24, Basel, Switzerland, Secretary General.

INTERNATIONAL UNION AGAINST TUBERCULOSIS, Rio de Janeiro, Brazil, Aug. 24-27. Prof. Etienne Bernard, 66 Blvd. St. Michel, Paris 6^e, France, Secretary-General.

LATIN AMERICAN CONGRESS OF PHYSICAL MEDICINE, Panama City, R. P., Feb. 24-29. Dr. Cassius Lopez de Victoria, 176 East 71st St., New York, N. Y., U. S. A., Executive Director.

NEURORADIOLOGIC SYMPOSIUM, Stockholm, Sweden, Sept. 17-20. Docent Ake Lindbom, Symposium Neuroradiologicum, Serafimerlasarettet, Stockholm K., Sweden, Secretary.

PAN-AMERICAN CONGRESS OF GASTROENTEROLOGY, Mexico City, D.F., May 11-17. Dr. R. Flores-Lopez, Calle Dr. Balmis, No. 148, Mexico City, D.F., Secretary.

PAN-EUROPEAN CONGRESS OF GASTROENTEROLOGY, Bologna, Florence and Rome, Italy, April 20-26. Prof. Guido Bassi, Policlinic of St. Orsola, Bologna, Italy, Secretary.

WORLD MEDICAL ASSOCIATION, Athens, Greece, Oct. 12-16. Dr. Louis H. Bauer, 2 East 103d St., New York 29, N. Y., Secretary General.

DEATHS

Sawyer, Wilbur A., Berkeley, Calif., died in the Samuel Merritt Hospital, Oakland, Nov. 12, aged 72, of arteriosclerotic heart disease. Dr. Sawyer was born in Appleton, Wis., Aug. 7, 1879. He received his medical degree from Harvard Medical School, Boston, in 1906. After serving an internship at the Massachusetts General Hospital in Boston, he joined the University of California as a medical examiner in 1908 and remained on the faculty until 1919, when he resigned. From 1914 to 1916 he was a lecturer and from 1916 to 1919 professor of hygiene and preventive medicine at the university. He was a director of the hygienic laboratory from 1910 to 1915 and from 1915 to 1918 secretary and executive officer for the California State Department of Public Health. During World War I he rose to the rank of major in the medical corps of the U. S. Army, serving as chief of the section on venereal diseases, Surgeon General's Office, War Department, as acting member of the interdepartmental social hygiene board, and as acting director of the social hygiene division of the commission on training camp activities. In 1919-1920 he was a lieutenant colonel in the medical reserve corps of the Army. Dr. Sawyer worked for many years with the Rockefeller Foundation. On June 1, 1919 he was appointed state director of the International Health Board of the Rockefeller Foundation, New York. He directed a hookworm campaign in Australia from 1919 to 1922 and from 1922 to 1924 was an adviser in public health to the Australian ministry of health. While there he was instrumental in organizing the Public Health Association in Australasia and was editor of *Health Forum*, which it published quarterly. He was an assistant regional director for the East from 1923 to 1924, and until 1927 he directed the foundation's public health laboratory service. Dr. Sawyer was a member of the West African Yellow Fever Commission of the foundation in 1926-1927 and, as associate director of the International Health Division, was in charge of the foundation's Yellow Fever Laboratory from 1928 to 1935. He is said to have prepared the first yellow fever vaccine. He became director of the foundation and served until 1944 when he retired. During the last four years he was director of the foundation's health commission. He was a member of the National Advisory Council of the U. S. Public Health Service from 1937 to 1940. During World War II, in addition to his work for the Rockefeller Foundation, Dr. Sawyer served as a member of the subcommittee on Tropical Diseases of the National Research Council, as director of the Commission on Tropical Diseases under the Army Epidemiological Board from 1940 to 1944, and as honorary consultant to the Medical Department of the Navy. From 1944 to 1947 he was a director of health of the United Nations Relief and Rehabilitation Administration. In 1948 he was secretary-general of the fourth International Congress on Tropical Medicine and Malaria in Washington, was convener in 1939 for the section Virus and Viral Diseases of the Third International Congress for Microbiologists, and in 1938 a delegate to the Pan American Sanitary Conference in Bogota. Dr. Sawyer was a member of the advisory scientific board, Gorgas Memorial Institute from 1944 to 1946 and since 1946 a member of the board of directors. In 1936 and 1937 he was president and at one time was vice-president of the American Academy of Tropical Medicine, in 1934-1935 president of the New York Society of Tropical Medicine, 1943-1944 president of the American Society of Tropical Medicine, and in 1918-1919 acting general secretary of the American Social Hygiene Association. Dr. Sawyer was a specialist certified by the American Board of Preventive Medicine and Hygiene, a member of the Society of American Bacteriologists, Association of American Physicians, American Association of Immunologists, American Society of Parasitologists, American Epidemiological Society, American Society for Experimental Pathology, Association of Military Surgeons of the United States, the Harvey

Society, Sigma Xi, and Alpha Omega Alpha; honorary member of the Societe Beige de Medicine Tropicale; corresponding member of the Societe de Biologie (Paris); and honorary life member of the Conference of State and Provincial Health Authorities of North America and the Tennessee Public Health Association. In 1926 he was cited Knight First Class Order of St. Olav (Norway) and in 1940 Gran Official Order of Carlos J. Finlay (Cuba). He won the first Leon Bernard Medal for his yellow fever research and medico-social protection to populations of many countries. The award was made in 1940 through the health committee of the League of Nations. At the meeting of the American Academy of Tropical Medicine Dr. Lewis W. Hackett of New York accepted the Richard Pearson Strong Medal for Dr. Sawyer four days following his death. In 1930 Dr. Sawyer delivered one of the DeLamar Lectures and in 1934 the third Harvey lecture. In 1945 he was awarded the LL.D. from the University of California.

Hayden, Reynolds Ⓔ Medical Director, Captain, U. S. Navy, retired, Chicago, died at the U. S. Naval Hospital, National Naval Medical Center, Bethesda, Md., Feb. 5, aged 68, of pulmonary hemorrhage. Dr. Hayden had been associated with the American Medical Association as a field representative of the Council on Medical Education and Hospitals since December, 1950. He was born in 1883 and received his degree of doctor of medicine from Georgetown University School of Medicine, Washington, D. C., 1905, and interned at Providence Hospital, Washington, D. C. During the Spanish-American War he was appointed acting past midshipman and served aboard the U. S. S. *Bennington*. On March 7, 1907 he was appointed assistant surgeon in the Navy and as a junior officer served at the Naval hospitals in Washington, D. C., Annapolis, Md., and Norfolk, Va., and with the Marine Contingent attached to the Army in the Cuban Pacification Campaign. Prior to World War I he served aboard the U. S. S. *Massachusetts* and the U. S. S. *Alert* and at the outbreak of World War I was serving at the Naval Academy. In 1918 he was on the staff of the U. S. military governor of San Domingo, where for three years he was in charge of the department of sanitation. He made the Australia cruise in 1925 as the senior medical officer aboard the U. S. S. *Seattle*. In 1927 he was ordered to the Naval Academy as the senior medical officer, where he served until 1940. Following his tour of duty at Pearl Harbor in 1942 he became the medical officer of the Third Naval District with headquarters in New York. Dr. Hayden was placed on the retired list of officers of the Navy on Oct. 1, 1946. He then engaged in medical writing in Washington. He was a fellow of the American College of Surgeons. Dr. Hayden received a letter of commendation from the Secretary of the Navy for his services as commanding officer of the U. S. Naval Hospital at Pearl Harbor at the time of the Japanese attack on Dec. 7, 1941. Other decorations include the Spanish-American War Ribbon, the Cuban Pacification Medal, World War I Victory Medal with Star, and a campaign badge for duty with U. S. Marine Expeditionary Forces.

Marshall, John Hugh Ⓔ Findlay, Ohio; born in Findlay, Ohio, Aug. 22, 1900; University of Louisville (Ky.) School of Medicine, 1925; fellow of the International College of Surgeons and the American College of Surgeons; member of the American Goitre Association; colonel in the medical corps of the U. S. Army Reserve; during World War II spent 33 months in the Asiatic Pacific theater and was awarded three Bronze Service Stars and a Distinguished Unit Citation; member of the city board of health; served on the staff of Findlay Hospital; chief-of-staff, Blanchard Valley Hospital; director and vice-president of the Findlay Rotary Club; died in Evanston, Wyo., November 12, aged 51, in a Union Pacific train accident.

Alenick, Daniel, Brooklyn; University of St. Andrews Conjoint Medical School, St. Andrews and Dundee, Scotland, 1934; on the staffs of the Kings County Hospital and Jewish Hospital, where he died Dec. 15, aged 47, of coronary thrombosis.

Ⓔ Indicates Fellow of the American Medical Association.

Batzes, Harry ⊕ New York; Fordham University School of Medicine, New York, 1914; affiliated with Samaritan Hospital in Brooklyn and Gouverneur Hospital; died Dec. 15, aged 65.

Campbell, Carl Herbert ⊕ Canfield, Ohio; Western Reserve University Medical Department, Cleveland, 1909; for many years president of the county board of education; served as president of the county board of health and the board of education of Canfield; a director and vice-president of the Farmers' National Bank of Canfield, and president of the Farmers Savings and Loan Bank of Canfield; died Nov. 16, aged 68, of coronary thrombosis.

Chambliss, Frank Mark ⊕ Xenia, Ohio; Eclectic Medical College, Cincinnati, 1926; served as mayor and city commissioner; died Dec. 14, aged 54, of coronary occlusion.

Clement, Samuel Anthony ⊕ Cambridge, Mass.; Boston University School of Medicine, 1914; member of the New England Pediatric Society; on the staff of Chester Hospital; on the courtesy staff of Mount Auburn Hospital; died Dec. 14, aged 64, of coronary thrombosis.

Draesel, Charles, North Bergen, N. J.; Kentucky University Medical Department, Louisville, 1906; served on the staff of North Hudson Hospital in Weehawken; died in Norwood Dec. 1, aged 83, of heart disease.

Earl, Warren Zachary, Los Angeles; University of Illinois College of Medicine, Chicago, 1913; formerly practiced in Sioux City, Iowa, where he was past president of the Woodbury County Medical Association and on the staffs of the Methodist and St. Joseph Mercy hospitals; died Nov. 19, aged 67, of dissecting aneurysm of the abdominal aorta.

Edler, William August ⊕ Pasadena, Calif.; Washington University School of Medicine, St. Louis, 1911; an Associate Fellow of the American Medical Association; formerly associate professor of neuropsychiatry at College of Medical Evangelists, Loma Linda and Los Angeles; specialist certified by the American Board of Psychiatry and Neurology; at one time affiliated with the U. S. Public Health Service Reserve; on the staff of the Collis P. and Howard Huntington Memorial Hospital; died Oct. 5, aged 51, of coronary occlusion.

Walter Sidney, Fordyce, Ark.; Memphis (Tenn.) Hospital Medical College, 1912; died in Little Rock Nov. 22, aged 68.

Fitzgerald, Robert Peter Francis, Irvington, N. J.; Temple University School of Medicine, Philadelphia, 1940; formerly affiliated with Veterans Administration Hospital in Lyons; member of the American Psychiatric Association; served during World War II; found dead Dec. 17, aged 35.

Gillis, John Ewen, Somerville, Mass.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1904; member of the American Medical Association; died Dec. 15, aged 72.

Hartinger, William Minx ⊕ Spring Valley, Ohio; Ohio State University College of Medicine, Columbus, 1916; died in Miami Valley Hospital, Dayton, Nov. 29, aged 57, of coronary occlusion.

Heeley, John Adelbert, Chillicothe, Ohio; Cleveland Homeopathic Medical College, 1908; member of the American College of Radiology; specialist certified by the American Board of Radiology; served during World War I; formerly on the staff of St. Joseph's Hospital in Warren; died in the Veterans Administration Hospital Nov. 28, aged 67, of rupture of the descending aorta and arteriosclerosis.

Jones, George William, Pomona, Calif.; University of Cincinnati College of Medicine, 1925; past president of the New Mexico Medical Society; served during World Wars I and II; on the staff of Pomona Valley Hospital, where he died Oct. 8, aged 51, of a heart attack.

Kittelson, Olaf, Zumbrota, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1912; served during World War I; a fellow at the Mayo Clinic in Rochester, Minn., for two years; on the staff of the Willmar (Minn.) State Hospital; died in Willmar Dec. 5, aged 64, of bronchial asthma with cerebral anoxia.

Lieblong, John S. ⊕ Greenbrier, Ark.; University of Arkansas School of Medicine, Little Rock, 1911; secretary and past president of the Faulkner County Medical Society; on the staff of Conway Memorial Hospital, where he died recently, aged 70, of acute coronary occlusion.

Look, Percy Jonathan ⊕ Andover, Mass.; Harvard Medical School, Boston, 1912; member of the New England Pediatric Society; formerly councilor of the Massachusetts Medical Society; past president of the Essex North District Medical Society; for many years chairman of the board of health of Andover; on the staff of the Lawrence General Hospital; died Dec. 9, aged 67.

Meinhardt, Maximilian, Chicago; Harvey Medical College, Chicago, 1903; died in Kenner Hospital December 1, aged 81, of hypostatic pneumonia and arteriosclerosis.

Murphy, James Augustine ⊕ Trenton, N. J.; Georgetown University School of Medicine, Washington, D. C., 1927; for many years on the staff of Mercer Hospital; died Dec. 5, aged 47, of cerebral hemorrhage.

Rowell, Edward Everett Jr., Greenwich, Conn.; Hahnemann Medical College and Hospital of Philadelphia; 1899; died December 2, aged 73, of a heart attack and lobar pneumonia.

Schroeder, Henry H., Verona, N. J.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1886; retired medical director of Mutual Life Insurance Company; formerly Essex Fells councilman; died Dec. 2, aged 90.

Shea, Timothy Thomas ⊕ San Francisco; Stanford University School of Medicine, San Francisco, 1915; on the staff of St. Mary's Hospital; died Dec. 2, aged 60, of coronary occlusion.

Sickley, Fred Leonard, Leonore, Ill.; Illinois Medical College, Chicago, 1904; served on the staff of St. Mary's Hospital in Streator; died December 2, aged 85, of coronary heart disease.

Tiffany, Braden Charles, Middlefield, Ohio; Cleveland Homeopathic Medical College, 1905; died Nov. 2, aged 72, of congestive heart failure.

Vaughan, John Russell, St. Louis; Washington University School of Medicine, St. Louis, 1910; member of the American Medical Association; certified by the American Board of Obstetrics and Gynecology; formerly member of the board of education in University City, Mo., where he had been president of the board for two years; served in France during World War I; formerly on the faculty of his alma mater; on the staff of St. Luke's Hospital, where he died Dec. 4, aged 63, of pneumonia.

Wallen, Benjamin Bertram, Wildwood, N. J.; Syracuse University College of Medicine, 1929; member of the American Medical Association; served during World War II; on the staff of the Burdett Tomlin Memorial Hospital, Cape May C. H., N. J.; died in Walter Reed General Hospital, Washington, D. C., Dec. 4, aged 48, of Hodgkin's disease.

Wheeler, John Tipton ⊕ Indianapolis; Eclectic Medical Institute, Cincinnati, 1889; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1907; an Associate Fellow of the American Medical Association; professor of anatomy at Indiana University School of Dentistry, retiring in 1940; served during World War I; for many years affiliated with Methodist Hospital, where he died December 4, aged 84, of cerebral hemorrhage.

White, Marcus Demosthenes ⊕ Ontario, Calif.; Washington University School of Medicine, St. Louis, 1920; past president of the San Bernardino County Medical Society; past president of the medical staff and member of the board of trustees of San Antonio Community Hospital in Upland; served during World War II; died Nov. 27, aged 57, of carcinoma.

Williams, Edward Charles, Port Trevorton, Pa.; College of Physicians and Surgeons, Baltimore, 1903; died in George F. Geisinger Memorial Hospital in Danville, Nov. 30, aged 70, of diabetes mellitus.

Wright, Frank O., Miami, Fla.; Baltimore University School of Medicine, 1897; died in St. Augustine, Oct. 16, aged 87, of hypostatic pneumonia.

GOVERNMENT SERVICES

ARMY

Exhibit of Pharmacopoeias.—An exhibit on the precursors of modern pharmacopoeias was shown in the Army Medical Library in February. An 1875 Leipzig printing of the oldest one, the Papyrus Ebers written about 1550 B. C. but incorporating much earlier material, now lost, was displayed. For each of the 700 remedies listed, the composition, dosage, method of administration, and the condition for which it is best suited are given. Some modern drugs, such as castor oil, opium, aloes, anise, and gentian, are shown to have been in use 3,500 years ago.

Also shown in the exhibit were Galen's work on drugs, the *Materia Medica* of Dioscorides, who acquired much of his knowledge of drugs while traveling with Nero's army, and Mesue's *Grabadin*, the translation into Arabic of the Greek and Latin pharmacopoeias. All of these works, and many others, were used as the basis for the municipal pharmacopoeias which developed with the rise of cities in the 15th and 16th centuries.

Of special interest in the exhibit was the little *Pharmacopoeia simpliciorum et efficaciorum in usum nosocomis militaris ad exercitum foederatarum Americae civitatum, 1778*. It was the first pharmacopoeia printed in the United States and was compiled for use in the Continental Army by Dr. William Brown, Surgeon in charge of the Continental Army Hospital at Lititz, Pa. The first American national pharmacopoeia appeared in 1820 and was compiled by medical school representatives meeting in New York City. Plans were made then for revising this pharmacopoeia every 10 years thereafter; our present U. S. P. is a direct lineal descendant of this early work.

Art Section of the Army Medical Library.—There are now more than 21,000 pictures and nearly 13,000 negatives in the art section of the Army Medical Library. Writers, editors, and publishing companies make frequent use of this picture material. The greatest number of calls are for portraits of physicians, military medical officers, nurses, historical material, hospital pictures, and medical subjects. This service to the public is steadily increasing. The library is grateful to receive additional pictorial material of medical interest. Gift pictures or information on pictures available for purchase should be addressed to the Catalog Division of the Medical Library, Seventh Street and Independence Ave., S. W., Washington, D. C.

PUBLIC HEALTH SERVICE

Fluoridation of Public Water Supplies.—A total of 173 communities have added fluorides to their water supplies as of Jan. 15, 1952, according to the Division of Dental Public Health. The population served by these water supplies is more than 4 million. The communities range in size from 100 persons (Mansfield, Conn.) to 424,683 (Indianapolis). The largest number of cities in any state is in Wisconsin, which has 64 communities fluoridating their water. More than 60% of these fluoridation programs were initiated within the past year, although three of them were begun in 1945.

New Chief of Division of Foreign Quarantine.—Dr. Calvin B. Spencer has been appointed chief of the division of foreign quarantine and Dr. Gilbert L. Dunnahoo chief of medical programs in Federal Security Agency Region 10, San Francisco. Dr. Spencer succeeds Dr. Dunnahoo in this FSA division. As chief of foreign quarantine, he heads the agency responsible for preventing the importation of infectious diseases into the United States and for the medical examination of aliens requesting admission into this country. The division operates 243 stations at seaports, airports, and points of border crossing in the U. S. and its possessions. Officers are also maintained at 24 U. S. embassies and consulates. During the past fiscal year, ending July, 1951, more than 31 million persons were checked by quarantine, and 28,000 planes and 20,000 ships were inspected. Not

one case of a quarantinable disease was imported into the country.

As chief of medical programs for FSA's Region 10, Dr. Dunnahoo will be responsible for programs on tuberculosis control, venereal disease, heart disease, cancer, environmental health, and public health nursing, which are now being operated in cooperation with the states and territories. Region 10 includes California, Arizona, Nevada, Oregon, Washington, Hawaii, and Alaska.

Foreign Students in the U. S.—With the start of the second term in the academic year, 13 physicians, dentists, and nurses from six foreign countries have come to the United States to study under the sponsorship of the Public Health Service in cooperation with the Mutual Security Agency and Point 4 programs. Of the 12 trainees, 5 are women and 8 men. They have come from Iran, Burma, Thailand, Greece, Mexico, and Brazil for periods of four months to one year. Four of the physicians are primarily interested in surgery, one in public health administration, one in serology, one in tuberculosis, and one in anesthesiology. Three of the women trainees are nurses, and the other two are dentists.

VETERANS ADMINISTRATION

New Hospital Managers.—Dr. Francis W. Ogg, chief of professional services at the Veterans Administration Center, Hot Springs, S. D., has been appointed manager of the center, succeeding Dr. Carl A. Neves, who retired Oct. 31. The Hot Springs Center consists of a hospital of 270 general medical and surgical beds and a domiciliary of 545 beds.—Dr. Linus A. Zink, manager of the new Brooklyn hospital, has been assigned in the same capacity to Mount Alto hospital, Washington, D. C., succeeding Dr. Charles M. Griffith who has retired after more than 34 years of government service.—Dr. J. Gordon Spendlove, chief medical officer, Veterans Administration Center, Fort Harrison, Mont., has been appointed manager of the Portland, Ore., VA Hospital effective February 1, succeeding Dr. Paul I. Carter who retired Jan. 31, 1952.—Dr. John B. McHugh, manager of the 162-bed Veterans Administration Hospital at Minot, N. D., will become manager of the 498-bed VA hospital at Kansas City, Mo., which is under construction. Dr. McHugh will succeed the late Dr. Willis M. Manney, who died in December, 1951.—Dr. George O. Pratt, manager of the VA hospital at Manchester, N. H., has been appointed manager of the VA Hospital in Brooklyn, succeeding Dr. Linus A. Zink who was transferred to the Mount Alto Hospital in Washington, D. C., where he is serving as manager.

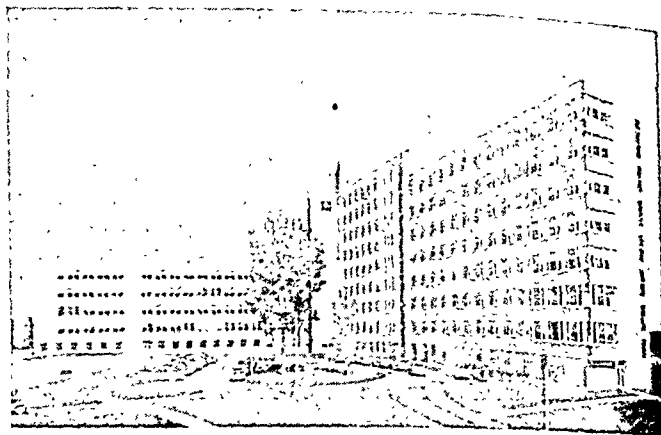
MISCELLANEOUS

Grants for Basic Research.—The National Science Foundation has approved 28 research grants, totaling \$410,000, in the field of the biological sciences. This is the initial group of grants that will be made under the foundation's program for support of basic research in the sciences. The total value of these grants represents slightly less than 40% of the funds available to the foundation for support of basic research for the current fiscal year. Additional proposals are being evaluated by the foundation with the advice of an advisory panel drawn from more than 50 outstanding American scientists.

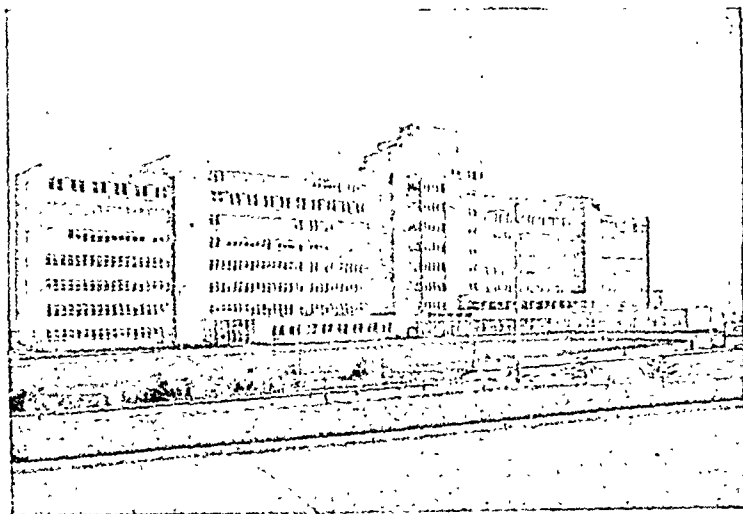
The research fields included are biochemistry, enzyme chemistry, biophysics, systemic biology, microbiology, aquatic biology, experimental embryology, genetics, immunology, experimental plant biology, and photosynthesis. The duration of grants in the initial group ranges from one to five years, with an average length of two and three-tenths years. The average grant amounts to \$6,300.

NEW VETERANS HOSPITALS COMPLETED DURING 1951

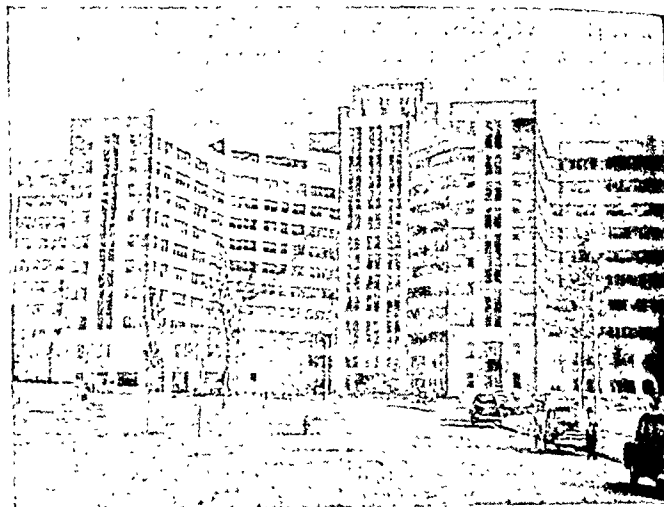
The new veterans hospitals illustrated on this page were completed during the calendar year 1951. As of Jan. 31, 1952, the Veterans Administration had 153 hospitals in operation, with a total bed capacity of 115,812; of these 31 were military and other hospitals transferred to the VA. Of the 153 hospitals, 20 were tuberculosis hospitals, 34 neuropsychiatric, and 99 general medical. As of that date, 24 new hospitals and 3 additions to existing hospitals with a total bed capacity of 15,440 and 1,192, respectively, were under construction; in addition 6 new hospitals with a total bed capacity of 5,000 and one addition to an existing hospital were in the planning stage. Illustrations of new veterans hospitals completed during the calendar years 1949 and 1950 appeared in *THE JOURNAL*, May 6, 1950, page 123, and March 10, 1951, page 748.



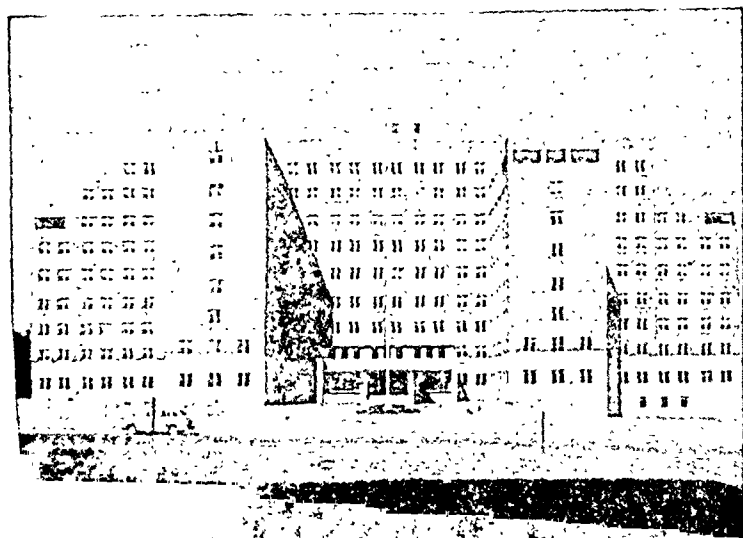
MADISON, WISCONSIN (500 beds)



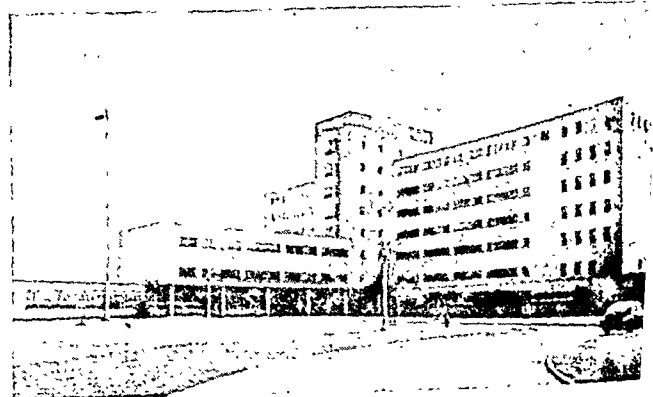
SEATTLE, WASHINGTON (300 beds)



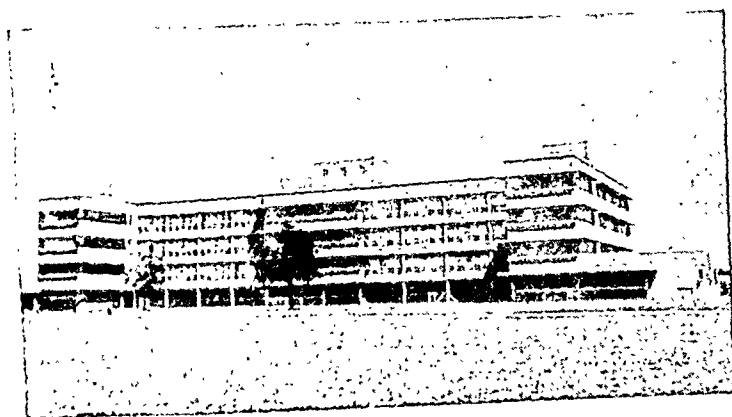
ALBANY, NEW YORK (1,000 beds)



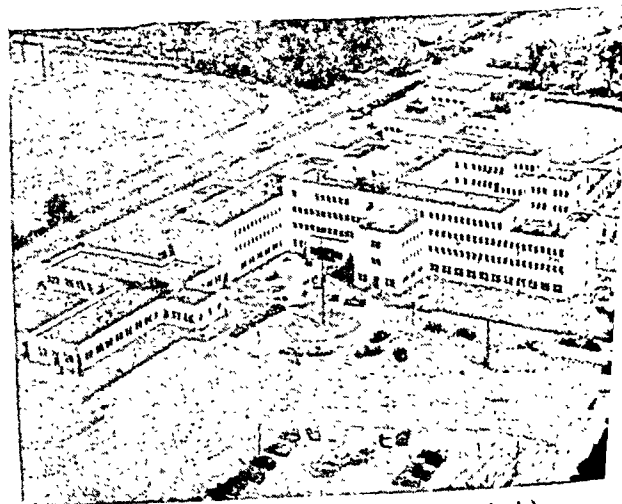
DENVER, COLORADO (500 beds)



ERIE, PENNSYLVANIA (200 beds)



BONHAM, TEXAS (350 beds)



PHOENIX, ARIZONA (200 beds)

FOREIGN LETTERS

RAZIL

Anal Anesthesia in Obstetric Cases.—Drs. B. Neme, J. Onofre Augusto, and B. Horo, of the obstetric department of Hospital das Clínicas, São Paulo State University, published an analysis of the use of anesthesia in 482 patients attended in that department. At first, the method of anesthesia chosen by the anesthesiology service frequently did not coincide with that indicated by the obstetrical department, but a better adjustment between the two services has been attained. The methods of anesthesia used in the 482 patients were categorized as follows: spinal anesthesia, 247 patients (51.3%); gas anesthesia, 161 (33.4%); local anesthesia, 58 (12.0%); and mixed anesthesia, 16 (3.3%). Of the 482 patients, there were 222 who had forceps delivery (46.0%), 208 who had cesarean section (43.2%), 27 patients with ectopic pregnancies (5.6%), 14 who had cranioclasia (2.9%), and 11 who had a uterine rupture (2.3%). Spinal anesthesia was used most often in cases in which forceps were applied. The authors point out that spinal anesthesia is being used oftener in cases of cranioclasia, particularly when forceps are used. An exception to the generalized use of spinal anesthesia is in cases of low fetal presentation.

The authors made a comparative study of the different methods of anesthesia and their relationship to blood pressure, the necessity of blood transfusion, and to neonatal asphyxia. Although arterial hypotension is one of the most undesirable effects of subarachnoid block, in 397 cases in which spinal anesthesia or gas anesthesia was used, the former method caused a drop in systolic pressure of 34.2 mm. of Hg against 36 mm. for the latter. According to the condition of the patient and the surgical procedure performed, the drops in systolic pressure were 29 mm., 39 mm., 30 mm., and 20 mm. Hg for spinal anesthesia and 31 mm., 46 mm., 36 mm., and 17 mm. Hg for gas anesthesia, in forceps application, cesarean section, cranioclasia, and ectopic pregnancy, respectively. According to the authors, the fewer number of patients needing blood transfusions is important proof that spinal anesthesia is the method of anesthesia best adapted to the physiology of parturition. In 5 cases in which spinal anesthesia or gas anesthesia was used in patients who had forceps application, cesarean section, or ectopic pregnancy, there was need of blood transfusion in 12.2% of the patients given the former method of anesthesia, whereas it was necessary in 22.3% of patients using the latter method. Neonatal asphyxia was present in 6.9% of the cases in which spinal anesthesia was used, whereas this rate was 11.8% for those who had gas anesthesia. There were no maternal deaths due to anesthesia.

The authors conclude by discussing the advantage of spinal anesthesia, especially the saddle block, for vaginal deliveries and emphasize that the ideal level for obstetric purposes is D_{11} - D_{12} for vaginal routes and D_6 - D_8 for abdominal obstetric surgery; they claim that a parallelism exists between the depth of the anesthesia obtained and the degree of hypotension present in the patient.

Efforts Toward Eradication of Anopheles Darlingi.—Dr. Fernando M. Bustamante, epidemiologist of the National Service of Malaria, reported to the Brazilian Malaria Association the results of the work done to exterminate *Anopheles darlingi*. *A. darlingi*, the most domestic species of the malaria vector mosquitoes in South America, comes into human dwellings in search of food. Despite the domesticity of this species, the frequency of *A. darlingi* attacking man and animals outdoors varies widely. This frequency, which defines the index of zoophilism of the species, is, in general, higher in Brazil than in Venezuela and British Guiana. In Brazil, the index of zoophilism of *A. darlingi* is higher in the central uplands than in the coastal lands. In consequence of this fact, the effect of DDT is

variable. Whereas, in Venezuela and British Guiana, this mosquito has or is being eradicated from great areas where the only antimosquito precaution is biannual house spraying, in Brazil, DDT did not produce the same result. *A. darlingi* is still being found in sprayed areas.

The possibility of eradication of *A. darlingi* depends on the tendency of this species to feed outdoors, the probability of eradication being inversely proportional to this tendency. Data given by the author for the coastal lowlands of the state of Rio de Janeiro and the central uplands of the São Francisco river valley give hope of eventual eradication of *A. darlingi* from the coastal districts, as it seems that this species is becoming scarce in the coastal districts of the state of Rio de Janeiro. It is not probable, however, that the same result can be obtained in the central uplands, where, in spite of spraying, *A. darlingi* continues to be caught either in the adult state or in the larval stage.

Heterologous Antibodies in Virus Hepatitis.—There is a need of other tests, besides clinical and histopathological data, for the diagnosis of virus hepatitis. Among the proposed serologic tests are the antiship hemagglutinins tests whose conclusions can only be accepted with important restrictions regarding the low agglutinin titers, the lack of absorption tests or details of technique, and the criterion for the corresponding clinical diagnosis.

In attempting to overcome these restrictions, Drs. Paulo de Goes and Clementino Fraga Filho, of Rio de Janeiro University, studied 36 samples of serums from patients who had clinical, laboratory, and histopathological diagnosis of virus hepatitis. The patients were tested for antiship hemagglutinins. The identification of these heterologous antibodies was based on their behavior as antigens in absorption tests with guinea pig kidney, rabbit kidney, ox heart, ox red cells (heated), and human liver (nonheated). Of the 36 serum samples, 26 (72.2%) showed an antiship titer of 1:56 or more, and 10 (27.8%) showed titers below that value. In nine of the samples, with titers 1:56 or higher, and, in five of those with a lower titer, an antibody was identified (H antibody) differing from those already described and showing the peculiarity of being removed (completely or almost completely) from all the antigens used. In three cases, the heterologous antibody behaved the same as the H antibody in absorptions with four of the antigens, differing only from one. Of the other 19 patients, 12 showed antibodies of known types, and, in 7, the antibodies were not identified. The highest antiship hemagglutinating titers and the H antibody were usually present in patients in whom the serums were tested 20 days after the onset of jaundice. Before this, the titers were usually low or did not show the typical behavior of the antibodies previously mentioned. In normal persons and patients with other diseases, heterologous antibodies, identical to those observed in some cases of virus hepatitis, were not found.

Pathogenicity of Shigella Quetta-454 in São Paulo.—During the past two years, isolations of *S.* and *Salmonella* have been made by the Public Health Department of Araraquara, state of São Paulo. In the second half of 1950, *shigella quetta-454*, Sachs (1943), was isolated on 19 occasions from persons suffering from diarrhea or dysentery and persons presumed to be carriers. Drs. Carlos S. Vernin and Ruy Soares of that city's public health laboratory are studying this micro-organism, which, as far as the authors know, is now being identified for the second time in Brazil. The author also reports clinical and laboratory data that may contribute to the knowledge of the pathogenicity of this species. Homologous antibodies were found in none of the cases. Twelve patients showed symptoms of diarrhea and dysentery, and two cases were complicated by the presence of trophozoites of *Endameba histolytica*. In 10 cases no other cause could be found, and the patients responded to treatment with sulfaguanidine, sulfadiazine, and succinylsulfathiazole (sulfasuxidine®). Six isolations were made from carriers without symptoms and one isolation was from an unclassified patient. New cases, which are still being found with the same etio and in the same area, are to be reported near fut

LONDON

The General Practitioner and the Hospital Service.—A report was published in response to a request by the secretary of state for Scotland to the Scottish Health Services Council, the statutory body that advises him on health service, to consider and advise him on the relationship between the general practitioner and the hospital service. This is a problem that has given increasing concern since the inauguration of the National Health Service. The report states that there is "an obvious need for a closer link between the general practitioner and the hospital and specialist services," and it calls for "early action" on several of its recommendations. "The general practice of the family doctor is the basis of a comprehensive medical service. The general practitioner must be much more than an agent to select patients for the nearest out-patient department or hospital, his own responsibility limited to the treatment of minor ailments." If the practitioner is to have time to devote to hospital work, some reorganization of general practice is required, e. g., by the provision of adequate secretarial help, the extension of group practice, and the possibility of the practitioner limiting his list of patients without loss of remuneration. A revision of the hospital and specialist organization is required, which will include physicians engaged in specialist practice, engaged in training for specialist practice, and engaged both in general and in specialist practice, and house officers. The practitioner undertaking part-time work in a hospital must be regarded as a member of the hospital team; he must not be regarded as a supernumerary member of the staff with no specific duties.

The principle to be established is that "there should be no barrier to the part-time employment in a specialist capacity, of the suitably experienced and qualified general practitioner." The fields in which there is scope for the part-time specialist include general medicine, pediatrics, geriatrics, dermatology, anesthetics, and ophthalmology. "There is also a strong case for the extended employment of general practitioners as clinical assistants, responsible under the charge of specialists for the regular care of patients and carrying out duties similar to those of registrars."

It is considered that "there is a very strong case for giving the practitioner the fullest scope for conducting the normal confinement of those of his patients who have booked for admission to hospital. . . . If practitioners generally are capable of supervising domiciliary confinements it can hardly be contended that they are incapable of conducting normal confinements in hospital. . . . If the present tendency to restrict the practitioner's part in institutional midwifery is not reversed there will undoubtedly be a decline in the standard of domiciliary practice . . . there is in fact a serious danger that midwifery will cease to be a basic part of general practice."

After reviewing all the arguments pro and con, the authors of the report "consider that there is a strong case for the provision of beds in which general practitioners can treat their own patients." For this purpose, hospitals are divided into three categories: cottage hospitals, district hospitals, and central hospitals. Cottage hospitals, i. e., small local hospitals, usually with 20 to 30 beds, should be maintained as general practitioner hospitals, and the fullest opportunity should be taken for regular visits by specialists. In district hospitals, i. e., general hospitals outside the main teaching centers, there is, at the moment, little scope for general practitioner beds. The same applies to central or teaching hospitals, but it is considered that there is much to commend the establishment of a general practitioner block associated with these large hospitals. In these, general practitioners would undertake the care of such patients as could not be treated at home but who did not need specialist treatment. Future policy should also envisage the setting up of general practitioner hospitals in suitable areas, organized as independent units but working in association with parent general hospitals providing a full range of specialist treatment.

Many other recommendations are made, dealing with such matters as increased access for general practitioners to ancillary services and refresher courses as well as attendance of general practitioners at ward rounds and outpatient sessions. The report has been accepted as one of the ablest and most practical that has yet been published in this country.

Electrical Safety in Hospitals.—It is announced in *Anaesthesia* that the Association of Anaesthetists of Great Britain and Ireland has been informed by the Ministry of Health that the Ministry of Health has appointed "two professional qualified electrical engineers who have had active experience in developing and applying the precautions and safe techniques lying within the engineering field in environments carrying explosive risks and whose duty it will be to advise hospital authorities on these related matters." These officers are to arrange a program of visits to hospitals throughout the country to discuss electrical problems with the appropriate members of the hospital staff such as surgeons, anesthetists, operating theater attendants, and engineers. In this way, they hope to promote improved engineering design and practice and "the development of materials suitable for use in hazardous environments and of equipment and appliances which provide greater intrinsic safety without sacrificing performance." They will also visit hospitals in which electrical accidents have occurred, so that they can discuss the matter with the staffs. In addition, they will advise the technical staffs of hospitals as to what plans are being worked out for construction, reconstruction, or equipping of operating theaters and labor rooms.

Shortage of X-ray Films.—In December a letter was sent to medical practitioners by the Chief Medical Officer of the Ministry of Health, drawing their attention to the serious shortage of x-ray film and appealing for their help in making the most possible use of the available supplies. He pointed out that the England usage during the first six months of 1951 was 16% greater than in the corresponding period of 1950 and 6% greater than in 1947. About the same time the President of the Board of Trade reported in Parliament that during 1951 the amount of x-ray film supplied to the home market was likely to be about 7½% more than during 1950, but that, in spite of this, difficulty was still being encountered in meeting demands from hospitals.

This serious state of affairs has given rise to many rumors as to the cause of the shortage. Both manufacturers and the ministry imply that the shortage is primarily due to increased demand, and the former deny that shortage of raw materials, faulty distribution, or increased export demands are responsible. On the other hand, the figures for export are impressive. In 1949 the amount of film exported during the 11 months from January to November, was 7,591,000 sq. ft. During the corresponding period in 1951 the figure was 13,997,000 sq. ft. The *British Medical Journal* points out, an average teaching hospital uses about 130,000 sq. ft. annually. The film exported in June, 1951, was 3,746,000 sq. ft. and would have supplied the needs of 28 teaching hospitals for a year.

Whatever the cause and actual supply situation, economies are called for, and in his letter the Chief Medical Officer appealed to hospitals to exercise strict economy in the use of film and to eliminate waste, particularly in processing. Practical suggestions which he advances to achieve this aim, include: (a) detailed specification by clinicians of the problem to be elucidated, the part to be examined, (b) spacing the reexamination of patients at longer intervals, (c) allowing only experienced clinicians and not junior house officers to make requests for x-ray examinations, and (d) reduction of the number of films used in one examination.

Whether further economies can be achieved is a matter of considerable debate. *The Lancet* considers that they can, the *British Medical Journal* states that "it is safe to say that further economy in x-ray departments will be very difficult to obtain." At the same time, the latter journal points out that considerable saving could be achieved by a greater use of miniature film in chest clinics, and it also reminds its readers that tomography is expensive in film, often with results that are not commensurate with this expenditure. The Joint Tuberculosis Council reports that any further deterioration in supplies will result in widespread impairment in the chest services and points out that one of the hazards of present-day radiology in this country is the electricity cuts that may lead to the spoiling of many films. Dr. J. F. Brailsford, the well-known Birmingham radiologist, on the other hand, believes that "a careful check of films used would show that wastage was in the region of 70% and often over 90%, and the tuberculosis and chest services

would top the list in waste." Out of the medley of conflicting views, three facts emerge. 1. There is a serious shortage of x-ray film at the moment. 2. This shortage is primarily due to increased usage since the introduction of the National Health Service. For instance, entirely apart from replacement of existing apparatus, 560 major x-ray units have been established in various clinics during the last two years. 3. Some degree of economy could be attained, provided clinicians were more precise and restrained in their demands and radiologists used the minimum number of films for any one patient.

SPAIN

Congress on Rheumatology.—The Second European Congress of Rheumatology was recently held in Barcelona. Prof. A. Pedro y Pons was president. Delegates from European countries, the United States, and Latin America were present. The inaugural speech was made by Dr. Barceló, secretary of the Congress. Other speakers were Prof. A. Pedro Pons, Professor Soriano, dean of the faculty of medicine at the University of Barcelona, Dr. W. S. C. Copeman, president of the European League Against Rheumatism, Dr. Ejnar Jarlov, president of the International League Against Rheumatism, Dr. A. Rjiz Moreno, delegate of the Pan-American League, and the governor of the city, who welcomed the delegates. Official topics were ankylosing spondylarthritis, ultrasonics, progress in endocrinology, non-articular rheumatism, and brucellar rheumatism.

Official speakers on ankylosing spondylarthritis were Drs. Forestier, Certonciny, Jacqueline, Rotés Querol, H. Van Swany, and J. Goslings. Bound copies of the papers concerning the clinical and roentgen aspects, pathology, and nosology of ankylosing spondylarthritis were distributed. Among the conclusions that were reached by the speakers were: 1. Ankylosing spondylarthritis is a chronic disease with three progressive phases: (a) a phase of development, with almost imperceptible limitation of the movement of the vertebral column, (b) a phase of establishment of the disease, with limitation of movement of the upper third of the vertebral column and an increasing limitation of movement of other vertebral segments, and (c) an advanced stage, with complete ankylosis of the vertebral column. 2. Diagnosis is based on the characteristic roentgen changes of the sacroiliac joints, which appear early. 3. Spondylarthritis, like progressive chronic polyarthritis and acute articular rheumatism, is a syndrome of unknown etiology. 4. Necropsy of three patients who had been under clinical observation for several years showed the typical diffuse proliferation of non-vascular cartilages in the intervertebral and sacroiliac joints, which leads to ankylosis of the cartilages.

Drs. A. Boni of Zurich and K. Matthes of Erlangen discussed ultrasonics. Dr. Boni said, "The mechanism of action of ultrasonics in treatment of rheumatic diseases is not clear. The basis of this treatment is largely empirical. Because of their sedative properties their use results in improvement of articular function and of muscular hypertonicity in degenerative rheumatism." Dr. Matthes reported that the effect of ultrasound on the human body is mainly due to the production of heat. The harmful effects of ultrasound obtained in animals are attributable to the use of excessive doses. Late lesions from application of ultrasound, comparable to those produced by roentgen ray therapy, never occur.

Dr. A. Robecchi of Turin, and Drs. Cirera Voltá, Pedro y Pons, Barceló Torrent, Vilaseca Sabater, Rotés Querol, and Batalia Boixet, all of Barcelona, discussed brucellar rheumatism. They reached the following conclusions: primary brucellar rheumatism may simulate other forms of rheumatism, arthritis, and spondylitis, caused by organisms other than *Brucella*, and may also resemble tuberculosis of the bones. The symptoms of primary brucellar rheumatism are similar to those of the osteo-articular complications of septicemic brucellosis; however, the symptoms of primary brucellar rheumatism are benign and reversible. A diagnosis is based on the following findings: brucellar spleen, positive results of the serum diagnosis, and favorable biologic response to the intravenous administration of brucellar antigens. The intravenous administration of increasing doses of brucellar lysates constitutes the specific cure for primary brucellar rheumatism of the locomotor system.

SWEDEN

Adoption of a Medical Code of Ethics.—The formal adoption of a medical code of ethics by the Swedish Medical Association, in 1951, is an event that necessitated much preparatory work. The World Medical Association is responsible for the new international code of ethics, and it is largely on this that the Swedish code has been modeled. It is pointed out, in an editorial note, in the Jan. 5, 1952, issue of *Svenska Läkartidningen* (the organ of the Swedish Medical Association) that the new code is neither reactionary nor revolutionary if the principles of western culture are held to be valid. The Swedish code consists of 15 rules; the first rule informs the physician that he must serve his fellow beings in conformity with the injunction to love one's fellow men. According to the fifteenth rule, the doctor must not participate in the care of the sick when he is not assured of complete freedom to act in conformity with medical rules; he must not deviate from those rules, even under the stress of a threat of serious consequences.

In conjunction with the new Swedish code, there is a radical revision of the conditions under which physicians may advertise. The Swedish Medical Association weighs the merits of each claim for advertising before endorsing it. There are 25 fields in which a Swedish doctor may specialize and about which he may publicly claim special knowledge. In addition to familiar fields of specialization, such as diseases of the eye, there are comparatively new fields, such as plastic surgery and disturbances of the voice and speech. In order to advertise that he is a specialist, a physician must show that he has spent five years in the post-graduate study of his specialty; for example, to call himself a bacteriologist and immunologist, he must prove that he has served three years in an authorized bacteriological laboratory, half a year in an infectious disease hospital, half a year in a general hospital, and another year in a special hospital for diseases such as tuberculosis or venereal disease.

The Late Professor Alfred Pettersson.—Dr. Alfred Pettersson, who was born on June 14, 1867, and died on Dec. 3, 1951, had a long and distinguished career as a bacteriologist. At first, he took an interest in ophthalmology and pathological anatomy, and it was not until the turn of the century that he began to devote his energy to bacteriology. Between 1907 and 1909, he was in charge of the bacteriological laboratory of the public health service of Stockholm. Between 1909 and 1919, he served as professor and director of a national bacteriological laboratory. In 1912, he was appointed professor of hygiene and bacteriology at the University of Uppsala. In 1918 and 1919, he was chairman of the Swedish Medical Society, and he edited the journal and transactions of this organization from 1919 to 1939. Since 1939, he has been an honorary member of this society. The many generations of medical students and physicians who were Professor Pettersson's pupils learned to appreciate his high standard of scientific sincerity. His logical thinking and incisive speech made him an effective teacher and an opponent to be respectfully encountered in debate.

Death of Professor Kahlmeter.—Dr. Gunnar Kahlmeter, who died last fall, played a distinguished part as Sweden's leading rheumatologist. He was born in Stockholm, on Aug. 10, 1885. In 1918 he took the degree of Doctor of Medicine, with a thesis on spondylitis deformans. He was put in charge of the Sabbatsberg Hospital in 1919. In 1925 he was made head of the Åsö Hospital, where he remained till 1945, when he was given charge of one of the medical departments of Södersjukhuset. He became a professor in 1946. His retirement in 1949 was due to failing health. While on the staff of the Government Pensions Organization he completed what was, perhaps, his most important work, a statistical analysis of the causes of invalidism. This work established his international reputation as a rheumatologist. He was the founder of the international organization La Ligue Internationale contre le Rhumatisme and was the recipient of various national and international honors. His scientific and popular publications largely concerned the problems of rheumatism.

TURKEY

Streptomycin and Sulfone Therapy in Leprosy.—Prof. Halil Gürün, Turkish dermatologist, graduate of Istanbul University, and currently of Kabul (Afghanistan) Medical School, has published the results of streptomycin therapy in 4 patients and of sulfone therapy in 10 patients with leprosy. The first patient was a man, aged 42. His body was covered with lepromas, and he had hoarseness, anesthesia, thermic anesthesia, and a profusion of Hansen bacilli in the lesions and nasal secretion. He was given an injection of 0.5 gm. of streptomycin twice daily for 10 days, which resulted in enlargement and softening of the lepromas, increase of hoarseness, and increase in Hansen bacilli in the nasal secretion. A few days later, ulceration occurred. A week later, i. e., 28 days after the initiation of the therapy, almost all lepromas had healed, and bacilli in the nasal secretion had decreased considerably. There was no intolerance, and the therapy was continued. During the following 37 days, the patient's condition further improved. After the administration of iodine, bacteriological examination proved the absence of Hansen bacilli. The therapy was continued. During the three months at the clinic, the patient received a total of 95 gm. of streptomycin. He insisted on being discharged but returned to Kabul 10 months later, at which time bacteriological examination confirmed the absence of Hansen bacilli. During this period there had been no clinical remission.

The second patient was a 34-year-old man from Turkistan. He was given a daily dose of 1 gm. of streptomycin for about three months, until he had received a total dose of 78 gm. Lepromas on the skin and Hansen bacilli disappeared. Since there was no law to enforce segregation, the patient left the clinic to return to his native Turkistan, but he purchased 100 gm. of streptomycin for his treatment there. Six months later he returned for reexamination, which revealed that he was free from clinical and bacteriological symptoms.

The third patient, a boy aged 14, was a native of Bisut, a Mongol Turkish colony and a district for lepers. The patient had large morphea alba patches on the heels and soles, atrophic scars on the body, anesthesia and thermoanesthesia on most of the skin, and Hansen bacilli in ulcerations and the nasal secretion. This patient was given 0.5 gm. of streptomycin daily for six months for a total dose of 92 gm. At the end of two months the ulcerating areas had healed, the morphea alba patches had regressed, and atrophy of the muscles subsided. By the end of the third month the patient was almost free from clinical manifestations; bacilli in the nasal secretion had completely disappeared, and they did not reappear during the rest of the treatment. Except for a few minor symptoms, there were no signs of intolerance. The patient was seen again seven months after discharge, and, on reexamination, no clinical or laboratory evidence was found.

The fourth patient, a 57-year-old native of Kabul, had swelling of the fingers and blisters on the hand, which developed into ulceration, and which had first appeared four years previously. He consulted a surgeon, who made a diagnosis of spina ventosa and did an operation, the result of which was severe deformities. Two years later red spots appeared on the patient's body, and the physician he consulted then made a diagnosis of syphilis and instituted treatment. When this did not improve the condition, the patient came to the outpatient department of the faculty clinic. Hansen bacilli in lesions and nasal secretion were profuse, and cicatricial atrophies exhibited a high degree of anesthesia and thermic anesthesia. As the patient insisted on ambulant treatment, he purchased 30 gm. of streptomycin and was given a daily dose of 0.5 gm. Even with this small dose, leprosy manifestations completely disappeared after two months, although the nasal secretion still showed Hansen bacilli. The patient could not afford more streptomycin, and, as he refused to enter a hospital, his treatment had to be continued with injections of chaulmoogra oil.

Of 10 adult patients with leprosy, who were given sulfone (disulon⁴) therapy, 6 had nodular leprosy, 3 had maculoanesthetic leprosy, and 1 had bone ulcers. All patients harbored Hansen bacilli. During the first six-day period the patients were given a daily dose of 75 mg. of disulon[®] during the second six-

day period 100 mg., and during the third, 125 mg. In several patients, vertigo, cyanosis, nausea, anorexia, and hemoglobinuria developed. In several patients the size of the lepromas increased, in several they took on a darker hue, in others they softened, and in others inflammation and infiltration developed around the nodules. There was a considerable increase in Hansen bacilli in the nasal secretion. The patients with maculoanesthesia did not respond. No drugs were administered during the fourth week, but during the fifth week each patient was given a daily dose of 175 mg. of disulon[®]. At the end of this period, lepromas on face and hands ulcerated, and eruptions appeared on the gums and in the mouth of two patients. In the other eight patients there was little change in the general condition or in the hemogram. During the seventh week the patients were given a daily dose of 200 mg. of disulon[®]. It was well tolerated by all patients, and at the end of the week Hansen bacilli in nasal secretions had greatly decreased, and in a few patients there were no bacilli at all. Administration of a small dose of iodine resulted in symptoms of intolerance, conjunctivitis, headache, and vertigo, demonstrating the incompatibility of iodine with disulon[®]. During the 9th, 10th, and 11th weeks, no drugs were administered. In the 12th week the patients were given a daily dose of 200 mg. of disulon[®] for three periods of six days. At the end of five months cicatrization of ulcers and absorption had occurred, Hansen bacilli in the nasal secretion were absent and few were found in the lepromas. The patients with maculoanesthesia had not improved markedly and are still under treatment. Professor Gürün will report later on his results with glucosulfone sodium (promin[®]), diasone[®] (disodium formaldehyde sulfoxylate diaminodiphenylsulfone), acetosulfone (promacetin[®]) and other sulfone preparations.

Medical Students at Ankara and Istanbul Universities.—Ankara and Istanbul universities opened for the year, Oct. 1, 1951. In an opening address, Prof. Ekrem Rushdi Izmen, rector of Ankara University, said that, whereas formerly the schools of law and literature had the highest enrolment of students, enrolment in the school of medicine has for several years exceeded theirs. However, lack of sufficient clinics, laboratories, and other equipment made it difficult to provide the students with practical experience. Because of the inflation, the 300-bed hospital erected by the Turkish Red Crescent Society for the establishment of a School of Nursing, has for years remained in a semi-finished state. This year, with £7,330,000 from the Marshall Plan, the hospital will be completed and equipped, and its clinics and laboratories will be opened to medical students.

At Ankara University there are 7,938 students, of whom 1,443 are women and 6,495 are men. The university has 15 professors, of whom 15 are foreigners, 87 associate and assistant professors, and 239 assistants. Since its establishment six years ago, Ankara University has conferred 66 doctor's degrees on graduates of the schools of law, letters, political science, agriculture, and 571 on graduates of the medical school; it has appointed 53 associate professors and conferred the degree of professor on 26 associate professors. Of the 1,050 new students admitted for the 1951-1952 period, 150 are medical students.

Prof. Kazim Ismail Gürkan, rector of Istanbul University, stated in his opening address that the university has 12,111 students, of whom 2,752 were women, 9,436 were men. There are 2,809 medical students. Since far more students seek admission to the university than can adequately be taken care of this year for the first time students were admitted on the basis of competitive examination; medical students were given medical aptitude tests.

On the staff are 136 *ordinarius* professors, 102 associate professors, 253 assistants, 34 lecturers, 5 interpreters at the disposal of the foreign professors, 6 monitors, 9 foreign lecturers, 10 foreign technicians, and 3 instructors, a total of 569 staff members. Of these, the medical school has 48 professors, 33 associate professors, and 134 assistants. The new allocations will be devoted to the establishment of a new psychology clinic and an orthopedic clinic. A new library will also be established. The new buildings for the School of Science and for the School of Literature are nearing completion; a pedagogy institute will be established. The chemistry institute will be transferred to the new building, and grounds will be set aside for a campus.

CORRESPONDENCE

DELIVERY OF BABIES AFTER FIFTY-FIVE

To the Editor:—I am appealing for help to learn the identity of a few of the women over the age of 55 who have given birth to babies. According to the National Office of Vital Statistics, such births number from 50 to 60 per year in this country. I have contacted this office, but they have no record by individual identity of these patients. I have contacted the Massachusetts Department of Vital Statistics and have found that birth certificates are filed chronologically but are not indexed by age. I am planning to write to registrars of vital statistics in other states along the Atlantic seaboard.

Would it be feasible to insert in *THE JOURNAL* an appeal to medical practitioners of the country at large as to whether any of them knows of bona fide cases of women over the age of 55 giving birth to children? It would be helpful, moreover, if birth certificates of these women were available as proof that the patients actually were of this stated age.

I would be extremely grateful if you can give me any help in this matter.

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LOW BODY TEMPERATURE

To the Editor:—Among the admirable data compiled by Laufman (*J. A. M. A.* [Nov. 24] 1951) in the emergency admission of a patient with unprecedentedly low body temperature, the metabolic rate of -7.8 appears impossible. Theory alone will rule out an energy exchange within normal limits at a hypothermia of 68 F (20 C), but supporting facts are as follows: 1. The demonstrated low metabolism of hibernation and of clinical and experimental hypothermia after the excitement stage. 2. The preservation of refrigerated bloodless extremities for 54 or 96 hours, and still longer survival of various grafts. 3. The record of 3 to 5 shallow respirations per minute, comparable to the observations in animals, could not have provided enough oxygen for life with normal metabolism. 4. Even if enough oxygen were inspired, the 12 to 20 feeble heartbeats per minute could not distribute it adequately. 5. Even if the oxygen were distributed, there is the additional difficulty of oxyhemoglobin dissociation at low temperature. 6. Minimal metabolism is the only explanation of the long survival of infant mammals with no respiration or heartbeat and of their long survival in nitrogen. Adolph, *Am. J. Physiol.* 155:366-377 [Dec. 1] 1948). 7. The very low return of warmth in Laufman's patient corresponds to observations in patients with known reduction of metabolism, and with normal metabolism the return would be more rapid. 8. Such extreme prolonged reduction of blood pressure and circulation, from trauma, hemorrhage, or any cause whatsoever must entail fatal shock if the metabolism is near normal. For these reasons the suppositions of elevation by alcohol ingestion or muscle tremors seem inadmissible. The specific dynamic action of foods at low temperatures is one of the interesting problems awaiting an investigator.

Besides the undesirability of allowing an impression that normal metabolism can prevail in mammals with low temperatures to enter the literature, two important considerations are involved. Assuming no errors of observation or calculation, inquiry concerning an artefact may be rewarding. The metabolism was tested when the respirations had risen to 16 per minute. The stimulation of breathing by the high blood acidity, perhaps to some extent also by the medication, might be conducive to an expumping of carbon dioxide retained from the preceding period of relative anoxia. It is pure speculation whether surplus oxygen could be used to compensate for anaerobic cell metabolism in that preceding period, perhaps by direct combination with incompletely oxidized products. A respiratory quotient

would be of interest, especially in view of the great hyperglycemia, but this also might be an artefact. The obscure physiology of hypothermia invites studies in species, such as the rat, which can tolerate these minimal temperatures. 2. A universal tradition erroneously lists cold among the causes of shock. Exhaustion due to voluntary efforts or shivering in the attempt to prevent chilling may predispose to shock, and subsequent frostbite lesions may directly produce shock, but the action of cold itself is to prevent or reduce shock by minimizing damage to tissues and vessels. This case of protection by systemic cold conforms to the many experiences of prevention of shock by local chilling of anoxic tissues. There should be wider application of this principle for traumatic shock and especially for burns.

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PROFESSIONAL JEALOUSY

To the Editor:—The American Medical Association has just completed two years of a strenuous campaign to foster and to promote better public relations with John Q. Public via the press and radio. It has made a gallant attempt to reawaken physicians so that American medicine can survive as a free and independent profession. It has attempted to remove a mysterious wall that sometimes has existed between physicians and the people in their community. It has tried to encourage physicians to participate more frequently in civic affairs and has so successfully stimulated such activities in many quarters that the communities now recognize physicians as human beings instead of as diagnostic machines. However, these energies expended by the American Medical Association to stimulate physicians to participate in community affairs may be doomed to at least partial failure unless the profession removes a problem from within its midst. This problem can be vicious and certainly is an unnecessary evil. Gossips speak of it as "professional jealousy." All physicians must admit that such an evil sometimes arises.

These two vilifying words have caused too many physicians to be reticent about participating in public relations programs such as those stressed by the American Medical Association. The fear of unjust and unwarranted criticism has prevented some influential physicians from supporting a program that requires their names in print. Regardless of the worthiness of the project, they fear some will misconstrue it as advertising.

Physicians as a rule are men of high academic and scholastic background, are of good moral character, and possess integrity. As one labor leader recently expressed himself: "Doctors are the type of rugged individuals who have built this country into what it is today. They must continue to use their freedom of speech to keep building America and to retain their own independence and self respect." Thus, where professional jealousy exists it must be eliminated, so that all physicians may be free to work in harmony with others to support the program of keeping American Medicine at the high level it has attained. It must be eliminated so that physicians need not fear unjust criticism.

The question arises "What can the medical profession do to eliminate professional jealousy?" It is our opinion that it could be eradicated to a great degree if the following suggestions were implemented.

A poll among physicians would probably reveal that untold numbers have never read the Code of Ethics of either the American Medical Association or the World Medical Association. The code should be read at a county level to all members during a regular monthly meeting. All physicians should receive a copy of it and of the oath of Hippocrates.

Physicians must realize and must let others realize that they are human beings and not diagnostic machines. They should have more round table discussions to receive constructive criticisms of themselves. Humility is an asset for all persons. Doctors should recognize the harm that can follow a lost temper and careless criticism of others, especially when the latter occurs in public,

Wholehearted support should be offered to civic projects by which the entire community benefits. All doctors, whether general practitioners or specialists, should try to recapture the respect that was once given to the "family doctor." No one should ever forget that "people who live in glass houses should not throw stones."

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PERFORATION FOLLOWING BARIUM ENEMA

To the Editor:—The danger of perforation of the colon proximal to a colostomy by self-administered irrigation through the colostomy stoma is well illustrated by the case reported by Drs. Earle I. Greene and J. Major Greene in *THE JOURNAL* (148:49 [Jan. 5] 1952). That this accident is a rare occurrence is borne out by the fact that the authors were able to find only one other report of a similar complication in the medical literature of the preceding 18 years. For this reason, and to illustrate still another and related means of perforating the bowel proximal to a colostomy stoma, I should like to record the occurrence of such an accident after barium enema study.

The patient was a white man, 50 years old, who had undergone abdominoperineal resection for rectal cancer on Aug. 24, 1945. Opaque material was introduced through the colostomy stoma on Sept. 10, 1946, to outline the remnant colon because of symptoms referable to the large bowel. To prevent regurgitation of the barium suspension, a balloon-tipped catheter was employed. Almost immediately after the balloon was distended and the flow of barium started, the patient complained of pain in the region just above the stoma. Roentgenograms obtained after introduction of barium, and again after an unsuccessful attempt to evacuate the clyisma, disclosed a sharp, short constriction of the splenic flexure but did not reveal a sinus tract or other evidence to indicate perforation of the bowel. Abdominal pain persisted and became still more pronounced after a saline enema self-administered by the patient in the hope of obtaining relief by emptying the colon of the previously introduced barium. The abdomen gradually distended, and tenderness and muscle guarding became apparent. The temperature rose to 100.3 F (oral) and the pulse rate to 108 beats per minute. Abdominal laparotomy was performed about 14 hours after the start of the barium enema study. A large perforation was found in the colon about 4 cm. proximal to the colostomy. Pelvic peritonitis was present, and plastic exudate covered the serosa of the small bowel. The perforated portion of colon was resected, and a section of bowel proximal to this was exteriorized as a new stoma. Recovery was slow, but the immediate postoperative course was otherwise uneventful.

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PERSISTENT COUGH DUE TO HAIR IMPINGING ON EARDRUM

To the Editor:—Every practitioner who deals with children is familiar with what has been called an "ear cough." This is produced by mechanical irritation of the membrana tympani during manipulation incident to clearing out the external auditory canal. Dried cerumen or foreign bodies introduced in the canal by children may be the cause of such reflex coughing, which is usually relieved by removal of the irritating substance whatever it may be. This communication is for the purpose of calling attention to a cause of such coughing that may easily escape notice if it is not suspected.

This cough reflex is mediated through the auricular branch of the vagus, which is distributed to the outer surface of the eardrum and through one or both of the laryngeal nerves. It is probably not produced by simple contact of a hair against the eardrum, unless the end of the hair definitely impinges on and irritates the drum. It is not uncommon to find one or more hairs lying against the drum without any resultant symptoms. When, however, the end of a hair is definitely pressed against the drum a most persistent and irritating cough can result.

This matter was first brought to my attention by Dr. Harmer B. P. Jordan, who was at that time assistant superintendent of the Charles V. Chapin Hospital. He described a child who was brought to the outpatient department because of a long-continued cough. Routine examinations did not reveal a cause until Dr. Jordan discovered in one auditory canal a hair imbedded in a mass of cerumen with its end against the drum. Removal of the hair was followed by complete relief of the cough. A year or two later a 13-year-old girl was brought to my office because of a severe dry hacking cough of two or three days' duration. Examination showed a hair impinging with one end on the eardrum. One month previously the hair had been noted to be curled against the drum. No symptoms were present at that time. Removal of the hair with ear forceps was followed by disappearance of the cough.

A few years later I mentioned this experience to Dr. Conrad Wesselhoeft of Boston, and shortly afterward he wrote me of a similar case in which several consultants had failed to determine the cause of a distressing cough in a child. He had discovered and removed a hair that was pressing against one of the eardrums. Removal of the hair cured the cough.

A fourth patient, seen in 1935, was a 27-year-old housewife, the wife of a physician, who had had a spasmodic cough for a month. It began, she believed, as a result of a mild upper respiratory infection. It had been completely resistant to various types of cough mixtures, including one containing 16 mg codeine to the teaspoonful. She had also been given phenobarbital. The cough had been nonproductive up to two days before she was seen. In talking the problem over with the patient's husband, mention was casually made of the cases of reflex cough from eardrum irritation by a hair, and, as the ear speculum was being withdrawn from what appeared to be a normal auditory canal, a hair, which had previously escaped attention, was seen lying on the floor of the canal with its end against the lower margin of the drum. This was carefully syringed out. The cough promptly disappeared.

While cough produced by this mechanism may well be familiar to many practitioners, no reference has been found in the literature consulted and the matter appears to be of sufficient interest to justify this report.

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ARTERIOVENOUS PULMONARY FISTULA

To the Editor:—Your editorial in *THE JOURNAL* of Jan. 12, 1952, on arteriovenous pulmonary fistula states, "A constant radiological finding is that of one or more nonprogressive pulmonary lesions that are seen as round masses, and which on fluoroscopic examination may be seen to pulsate."

We are reporting two cases in which pulmonary arteriovenous aneurysm were looked for ante mortem with x-ray and fluoroscopy and were not seen. The lesions may be so situated that these methods fail to reveal the lesion and they are brought to light only by angiography.

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ELI LILLY MEDICAL RESEARCH FELLOWSHIP (SOUTH AFRICA)

To the Editor:—I should like, through the courtesy of your columns, to draw the attention of medical practitioners registered in South Africa who may at present be in the United States to the fact that applications may be submitted for the 1952 award of the Eli Lilly Medical Research Fellowship. Further details can be obtained from the address below. The closing date for applications is May 8, 1952.

L. EALES, Honorary Secretary,
Selection Committee Eli Lilly Medical
Research Fellowship
Cape Town Post-Graduate Medical Association
P. O. Box 2980, Cape Town, South Africa.

BUREAU OF LEGAL MEDICINE AND LEGISLATION

MEDICOLEGAL ABSTRACTS

Group Hospitalization.—Osteopathic Hospital as "Nonmember Hospital" Under Membership Contract.—The plaintiff filed suit against the defendant, Group Hospital Service, Incorporated, to recover the cost of hospital services rendered to his wife. From a judgment in his favor, the defendant appealed to the court of civil appeals of Texas.

The plaintiff owned a policy issued by Group Hospital Service, Incorporated, which entitled him and his wife to certain benefits agreed upon therein. His wife, having suffered a stroke, was carried to an Osteopathic Hospital and was there treated by a Dr. Vick, who had studied at Kirksville College of Osteopathy and who held a license to practice medicine in Texas, but who was not the holder of an M.D. degree. After leaving the hospital, the expense of hospitalization and treatment received therein was submitted in a claim to the defendant; liability was denied by reason of a provision in the membership agreement which defined a nonmember hospital as one registered with the American Medical Association. As a condition to registration with the American Medical Association, a hospital is required to meet a number of rules designed to raise the standard of service to the patients in the hospital, one of such rules being: "Osteopaths, Chiropractors, and other non-medical practitioners may not be permitted to use the facilities of hospitals desiring to conform to these standards." It was conceded that the Osteopathic Hospital was not registered with the American Medical Association and that Dr. Vick was not permitted to practice in hospitals registered with the American Medical Association.

The plaintiff contended that the provision in the membership agreement requiring nonmember hospitals, as a minimum requirement, to be registered with the American Medical Association was in violation of Section 5, Article 4590a of the state statutes and that this clause in the contract resulted in the defendant's controlling the relation existing between the member and his or her physician and restricting the right of the plaintiff to obtain the services of any licensed doctor of medicine. Article 4590a, said the court, does not attempt to compel the defendant to enter into a membership contract with any hospital, nor does it attempt to compel any hospital to enter into a contract with the defendant. Thus, the defendant had the right to contract with any hospital, or group of hospitals, with whom it chose to deal as member hospitals. Nowhere in the application of the plaintiff or in the contract of membership issued to him, is found any expression that might be interpreted as evidence that the defendant was attempting to practice medicine in any manner or to furnish to the plaintiff a physician or any medical service. It is also significant and accepted that there is neither in the plaintiff's application nor in his contract of membership any express contract provision prohibiting osteopaths or any other type of practitioner from treating or serving any member hospitalized in either a member hospital or a non-member hospital.

Section 5 provides, in part, ". . . but said corporation shall confine its activities to rendering hospital service only through such type of hospitals with whom it has contracts." If we are to give any effect to this clear provision of the statute, said the court, it is evident that a limitation is being placed on the activity of the corporation. What is the limitation so placed? The answer is evident that the corporation shall render hospital service only through such type of hospitals with whom it has contracts. And the final question would be, "What type of hospitals does Group Hospital Service, Incorporated, have contracts with?" In the case at bar it is uncontroverted that Group Hospital Service, Incorporated, has contracts only with hospitals registered with the American Medical Association. Since Group Hospital Service, Incorporated, has contracts only with hospitals registered with the American Medical Association and a right to so contract is permissible under the statutes, it would clearly appear that the corporation was not contracting in violation of the statute but was, in fact, contracting strictly within the statute by "confining

its activities to rendering hospital service only through such type of hospitals with whom it has contracts."

Since Group Hospital Service, Incorporated, as a nonprofit organization entered into a written contract with the plaintiff to furnish hospitalization benefits to the plaintiff and his wife through nonmember hospitals who were registered with the American Medical Association and has confined its activities to rendering hospital service only through such type of hospitals, the fact that such type of hospitals have valid rules which might exclude certain physicians will not place the membership agreement executed by the plaintiff and the defendant in violation of any section of the statute. Accordingly the judgment of the trial court in favor of the plaintiff was reversed and judgment was entered in favor of the defendant Group Hospital Service, Incorporated.—*Group Hospital Service, Incorporated v. Armstrong*, 240 S. W. (2d) 418 (Texas 1951).

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

ADDITIONAL HOSPITALS REGISTERED

The following hospitals were registered by the Council on Medical Education and Hospitals of the American Medical Association at its meeting in Chicago, Feb. 9, 1952:

DeKalb County General Hospital, Fort Payne, Ala.	Ivy Memorial Hospital, West Point, Miss.
Phoenix Medical Center (General), Phoenix, Ariz.	Pemiscot County Memorial Hospi- tal, Hayti, Mo.
White Mountain Hospital, Spring- ville, Ariz.	Teton Memorial Hospital, Choteau, Mont.
Memorial Hospital, Arkadelphia, Ark.	Garfield County Hospital, Jordan, Mont.
Gray Memorial Hospital, Little Rock, Ark.	Malta Hospital, Malta, Mont.
Piggott Hospital, Piggott, Ark.	Otto Maternity Home, Bloomfield, Neb.
Alta Local Hospital, Dinuba, Calif.	Perkins County Community Hospi- tal, Grant, Neb.
Sister Kenny Polio Hospital, El Monte, Calif.	Our Lady of Lourdes Hospital, Camden, N. J.
Holy Cross Hospital, Los Angeles, Calif.	Neponsit Beach Hospital, Neponsit, N. Y.
John C. Fremont Hospital, Mari- posa, Calif.	Institute of Physical Medicine and Rehabilitation, New York, N. Y.
The Westerly, Verice, Calif.	Mercy Memorial Hospital, Urbana, Ohio
Westwood Hospital, Westwood, Calif.	Clinton Memorial Hospital, Wil- mington, Ohio
Motion Picture Country Hospital, Woodland Hills, Calif.	Federal Reformatory Hospital, El Reno, Okla.
Baptist Hospital, Pensacola, Fla.	Okfuskee County Hospital, Oke- mah, Okla.
South Sarasota County Memorial Hospital, Venice, Fla.	Curry Hospital and Clinic, Sapulpa, Okla.
Terrell County Hospital, Dawson, Ga.	Lakeview Hospital, Lakeview, Ore.
Eureka Hospital, Eureka, Ill.	F. W. Black Community Hospital, Lewistown, Pa.
Mendota Community Hospital, Mendota, Ill.	Self Memorial Hospital, Green- wood, S. C.
Martin's Convalescent Home, Peoria, Ill.	Giles County Hospital, Pulaski, Tenn.
Community Hospital, Bremen, Ind.	Polk County Hospital, Corrigan, Texas
Buffalo Center Hospital and Clinic, Buffalo Center, Iowa	Waller County Hospital, Hemp- stead, Texas
Rock Rapids Hospital, Rock Rapids, Iowa	Polk County Hospital, Livingston, Texas
City Hospital, Sheldon, Iowa.	Muenster Clinic and Hospital, Muenster, Texas
Achenbach Memorial Hospital, Hardtner, Kan.	Cochran County Hospital, Morton, Texas
Pratt County Hospital, Pratt, Kan.	Throckmorton County Memorial Hospital, Throckmorton, Texas
District Four State Tuberculosis Hospital, Ashland, Ky.	Medical Center Hospital, Tyler, Texas
Mercer General Hospital, Harrods- burg, Ky.	Okanogan County Hospital District No. 1, Brewster, Wash.
Notre Dame Hospital, Lynch, Ky.	Olympic Memorial Hospital, Port Angles, Wash.
U. S. Naval Hospital, Bainbridge, Md.	Algoma Memorial Hospital, Algoma, Wis.
Hayes-Green-Beach County Memo- rial Hospital, Charlotte, Mich.	Capitol Hospital, Milwaukee, Wis.
Community Memorial Hospital, Clarkfield, Minn.	Tigerton Hospital, Tigerton, Wis.
Murray County Memorial Hospital, Slayton, Minn.	Doctors Hospital, Santurce, P. R.
Worthington Municipal Hospital, Worthington, Minn.	
Covington County Hospital, Collins, Miss.	

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Arch. Internal Medicine, Chicago

88:701-848 (Dec.) 1951

- *"Idiopathic" Thrombocytopenia: Review of 89 Cases with Particular Reference to Differentiation and Treatment of Acute (Self-Limited) and Chronic Types. E. O. Hirsch and W. Dameshek.—p. 701.
- Moniliasis in Patients Treated with Aureomycin: Clinical and Laboratory Evidence that Aureomycin Stimulates Growth of *Candida Albicans*. R. B. Pappenfort Jr. and E. S. Schnall.—p. 729.
- *Cat-Scratch Disease: Nonbacterial Regional Lymphadenitis. W. B. Daniels and F. G. MacMurray.—p. 736.
- Rationale of Therapeutic Use of Streptokinase-Streptodornase in Amebic Abscess of Liver. S. Sherry, W. R. McCarty and W. S. Tillett.—p. 752.
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- Diagnosis of Dissecting Aneurysm of Aorta. C. A. Domzalski Jr.—p. 770.
- Chronic Scleroderma with Acute Exacerbation During Corticotropin Therapy: Report of Case with Autopsy Observations. J. H. Lunseth, L. A. Baker and A. Shifrin.—p. 783.
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- Hypocellular Marrow in Acute Leukemia: Report of Two Cases. M. R. Beyers, L. M. Meyer, M. Lowenthal and others.—p. 803.
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- Asbestosis Associated with Bronchogenic Carcinoma. R. Stoll, R. Bass and A. A. Angrist.—p. 831.
- Coarctation of Abdominal Aorta Simulating Pheochromocytoma. J. W. Goldzieher, H. E. McMahon and M. A. Goldzieher.—p. 835.
- *Combined Antibiotic Therapy: Report of Case of Subacute Bacterial Endocarditis Reinfected with Diphtheroid and Successfully Treated with Penicillin and Bacitracin. R. Wallach and N. Pomerantz.—p. 840.

"Idiopathic" Thrombocytopenia.—On the basis of thrombocyte counts obtained during remissions in 89 cases of "idiopathic thrombocytopenic purpura," two clinical types of "idiopathic" thrombocytopenia could be distinguished: acute, self-limited thrombocytopenia in 26 cases, and chronic thrombocytopenia in 55 cases. In the former, spontaneous recovery usually occurs within four months of the onset. In the latter, while clinical remissions are also the rule, thrombocytopenia persists and exacerbations are common. The two types differ in their modes of onset, the presence or absence of etiological factors, the occurrence of eosinophilia and lymphocytosis, incidence of splenomegaly, and tendency to be familial. On the basis of these features it is usually possible to distinguish the two entities; of the authors' 89 cases, only 8 were unclassified. The diagnosis of thrombocytopenia, particularly of the chronic idiopathic type, must be considered whenever excessive bleeding is present, even in the absence of petechiae or purpura. In evaluating therapy it is necessary to differentiate clearly between acute, self-limited thrombocytopenia and the chronic disease. In acute thrombocytopenia the evaluation of any treatment, including splenectomy, is frequently impossible because of the self-limited nature of the disease. In chronic idiopathic thrombocytopenia, because of the frequency of spontaneous clinical remissions that often are of many years' duration, and because of the spontaneous fluctuations in thrombocyte count, treatment can be

considered successful only if the thrombocyte count is normal over a significant time. Splenectomy may be considered curative only if the thrombocyte count remains normal for at least four to six months after operation. Although the decision for or against splenectomy is still difficult in an individual case during an attack of acute purpura, the authors' data suggest that it may be best to treat such episodes by supportive measures and to perform splenectomy only after frank purpura has subsided. On the other hand, local bleeding from mucous membranes often responds dramatically to splenectomy and, if unaccompanied by purpura, should not be considered a contraindication to the operation. Splenectomy resulted in the cure of about two thirds of the patients with chronic idiopathic thrombocytopenia. Because of the low mortality of this operation when patients are free of purpura and the possibility of future hemorrhagic crises, splenectomy should be done in all patients with chronic idiopathic thrombocytopenia as soon as the diagnosis is established and the patient is free of purpura. Splenectomy is probably of no value in thrombocytopathic thrombocytopenia. There were too few cases of acute thrombocytopenia to permit definite conclusions concerning the value of splenectomy in modifying the course of acute thrombocytopenia.

Cat-Scratch Disease.—More than 100 cases of sterile suppurative regional adenitis associated with fever and constitutional symptoms in persons who had been scratched by or had contact with cats have been reported in the literature. The authors report 12 additional cases in persons between the ages of 10 and 73. All had had more or less intimate contact with cats; seven had been scratched and one bitten. Transmission of the disease by insect bite was probable in one instance. Inhalation of infectious material was suggested in one patient who had sore throat associated with massive cervical lymphadenopathy. This followed the sniffing of pillows soiled by cat urine to determine whether they had odor. Five of the patients had primary lesions at site of inoculation in the form of a scratch scar covered by scabbed erythematous papule. These lesions appeared within one to four days of the time of inoculation. The lymphadenopathy involved the cervical nodes in 4 patients, the femoral or inguinal nodes in 3, and the epitrochlear and axillary nodes in 5. In patients with enlargement of cervical nodes the supraclavicular nodes were also involved in three, the occipital nodes in one, and a submental node in one. None of the patients was seriously ill. Mild to moderate fever was noted in about half of the patients. Systemic symptoms, consisting of chills, headache, and generalized aching, occurred in three instances. Leukocyte counts were normal in the six patients in whom they were made. An anti-toxin prepared from the aspirated pus by Hanger and Rose, one of whom himself had cat-scratch disease, was used for intradermal tests on the authors' patients; the test was found to be specific. The evidence indicates that the disease is ubiquitous and is frequently confused with more serious illness. The disease is usually self-limited, lasting from weeks to months. The lymph nodes have a characteristic microscopic pattern that is suggestive but not diagnostic. The causative agent is unknown.

Combined Antibiotic Therapy.—A woman aged 28 with subacute bacterial endocarditis due to *Streptococcus viridans* who subsequently became reinfected with a diphtheroid was treated intermittently with penicillin, then aureomycin, and later streptomycin. Each of these agents proved to be ineffective. The blood stream was finally sterilized permanently by the combination of penicillin (in doses of 6,000,000 to 12,000,000 units daily) and bacitracin (in doses of 30,000 to 80,000 units daily) for 10 days. In vitro sensitivity tests, using combinations of penicillin and streptomycin and of penicillin and bacitracin, showed synergism against the organisms tested. An objectionable feature of the parenteral use of bacitracin is the high incidence of nephrotoxicity. It is suggested that parenteral treatment with bacitracin might be of value when bacitracin is used in smaller doses in combination with penicillin for its synergistic effect.

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Titles marked with an asterisk (*) are abstracted.

American Journal of Medical Sciences, Philadelphia

222:485-612 (Nov.) 1951

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- Diagnosis of Tertiary Syphilis of Liver: 25 Years After McCrae.** E. Shapiro and H. Weiner.—p. 494.
- Mortality of Acute Myocardial Infarction in Private Practice.** S. Baer, W. I. Heine and S. O. Krasnoff.—p. 500.
- Effect of Acidosis and Alkalosis on Plasma Potassium Concentration and Electrocardiogram of Normal and Potassium-Depleted Dogs.** W. B. Abrams, D. W. Lewis and S. Bellet.—p. 506.
- Reappearance of Abnormal Laboratory Findings in Rheumatic Patients Following Withdrawal of ACTH or Cortisone (with Special Reference to C-Reactive Protein).** S. R. Ziegler and A. G. Kuttner.—p. 516.
- Anti-Rheumatic Effects of 3-Hydroxy-2-Phenylcinchoninic Acid (HPC) in Gout, Rheumatic Fever, and Rheumatoid Arthritis.** J. Simson and J. J. Bunim.—p. 523.
- Hepatic Function Tests in Weil's Disease.** A. B. Shinn, H. P. Roth and R. D. Moore.—p. 530.
- Osmotic Erythrocyte Fragility in Patients with Jaundice.** E. R. Movitt, B. Gerstl and E. A. McKinlay.—p. 535.
- Antidiuretic Hormone Studies in Patients Presenting Edema.** M. Dochios and L. S. Dreifus.—p. 538.
- Afferent Loop Studies After Subtotal Gastric Resection.** S. H. Lorber and H. Shay.—p. 544.
- Ebstein's Disease: Report of First Case Diagnosed During Life.** L. A. Soloff, H. M. Stauffer and J. Zatuchni.—p. 554.
- Recurrent Thrombophlebitis: Experimental Study of Life Situations and Emotions and Clotting Time and Relative Viscosity of Blood.** R. A. Schneider.—p. 562.
- Chronic (Non-Specific) Ulcerative Colitis: Review of Medical Therapy.** T. E. Machella.—p. 579.
- Peptic Ulcer in Children.** R. H. Morgan.—p. 590.

Recurrence of Abnormal Reactions Following Withdrawal of Corticotropin or Cortisone.—Investigators had observed that the serums of acutely ill patients gave a precipitin reaction with a non-type-specific polysaccharide isolated from pneumococcus cells. This reaction has been found to be due to a protein not normally present in blood, the C-reactive protein, which also provides a sensitive test for rheumatic activity. Ziegler and Kuttner therefore decided to study the C-reactive protein in children with rheumatic carditis treated with corticotropin (ACTH) or cortisone. They found that the C-reactive protein was present in 16 children with signs of rheumatic carditis before treatment was instituted, but usually decreased rapidly with hormone therapy. The abrupt withdrawal of corticotropin or cortisone early in the course of therapy was usually followed by a prompt recurrence of rheumatic manifestations, but even when these hormones were withdrawn gradually after a prolonged course of therapy, it was found in many instances that the C-reactive protein level as well as the erythrocyte sedimentation rate and gamma globulin again became abnormal. Some patients in whom clinical evidence of carditis failed to subside during therapy received more than one course of treatment. Rebound phenomena were observed after each course. Despite apparently adequate treatment, only one patient in this series showed no clinical or laboratory evidence of rheumatic activity when therapy was discontinued. One patient had a clinical relapse and 14 showed various abnormal laboratory findings shortly after cessation of treatment. The "laboratory" rebound phenomena did not appear to be due to the fact that rheumatic fever was polycyclic, since they subsided promptly without further treatment, usually within two or three weeks. A possible explanation of rebound phenomena might be that following withdrawal of corticotropin or cortisone, the response of the body is altered, probably because of temporary depression of adrenal function. If the rheumatic process has not subsided completely, this decreased adrenal activity tends to make various laboratory tests more strongly positive than they would be at the same time in the natural course of the disease. The authors suggest that it is not advisable to resume treatment until sufficient time has elapsed to determine whether or not the abnormal laboratory findings will return to normal spontaneously.

Anti-Rheumatic Effects of 3-Hydroxy-2-Phenylcinchoninic Acid.—Simson and Bunim used 3-hydroxy-2-phenylcinchoninic acid (HPC) in treatment of 4 patients with gout, 10 with rheumatoid arthritis, and 6 with rheumatic fever. The drug was given in doses varying from 20 to 40 mg. per kilogram of body weight. All but two patients were started on the smaller dose, and, when symptoms persisted, the dose was increased to 30 and in some cases to 40 mg. The total daily dose was given in three equal

portions after each meal or at hourly intervals after breakfast. The drug was administered for from 5 to 35 days. The total amount given varied from 5.4 gm. to 81.4 gm. The administration of 3-hydroxy-2-phenylcinchoninic acid was followed by pronounced improvement in the arthritis of gout. In three subjects the response was as satisfactory as that obtained with colchicine but in the fourth colchicine induced a more rapid subsidence of symptoms. In rheumatic fever marked improvement in polyarthritis, fever, and general malaise was observed. The degree and rapidity of response were comparable to those achieved with salicylate therapy. The effects on rheumatic carditis could not be determined, since none of the patients had heart disease. In most of the patients with rheumatoid arthritis, improvement in articular symptoms was comparable to that noted with salicylates but not to that obtained with cortisone or corticotropin. In 3 of 10 patients relief was greater with 3-hydroxy-2-phenylcinchoninic acid than with salicylates; in 2 no benefit was obtained. One or more toxic reactions were noted in 16 of the 20 patients treated. Most of these were mild, but in four patients side-effects necessitated interruption of therapy. The anti-rheumatic effect of this acid appears to be no greater than that of salicylates in acute rheumatic fever or rheumatoid arthritis. Since in gouty arthritis 3-hydroxy-2-phenylcinchoninic acid is about as effective as colchicine, it may be useful in gouty patients who do not tolerate or who are resistant to colchicine.

Annals of Internal Medicine, Lancaster, Pa.

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- Endocrine Patterns During Aging.** T. H. McGavack.—p. 961.
- Medical Problems in Radiological Defense.** F. R. Philbrook.—p. 975.
- Evaluation of Antibiotic Therapy in Human Leptospirosis.** H. E. Hall, J. A. Hightower, R. D. Rivera and others.—p. 981.
- Psychosomatic Medicine Looks at Medical Specialization.** S. Rubin.—p. 999.
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- Blood Pressure Variations in the Two Arms.** M. J. Rueger.—p. 1023.
- Use of Vitamin B₁₂ in Management of Neurologic Manifestations of Diabetes Mellitus, with Notes on Administration of Massive Doses.** S. M. Sancetta, P. R. Ayres and R. W. Scott.—p. 1028.
- Oculo-Oro-Genital Syndrome: Deficiency Disease.** E. C. Jacobs.—p. 1049.
- Revitalization of Tissue and Nutrition in Older Individuals.** W. B. Kountz.—p. 1055.
- Coccidioidal Meningitis: Report of Four Cases with Necropsy Findings in Three Cases.** V. E. Jenkins and J. C. Postlewaite.—p. 1068.
- Intermittent and Transient Bundle Branch Block: Clinical and Electrocardiographic Study.** A. A. Sandberg, J. Wener, A. M. Master and L. Scherlis.—p. 1085.
- Liver Function: Attempt to Correlate Structural Change with Functional Abnormality.** J. W. Norcross, J. D. Feldman, R. F. Bradley Jr. and R. M. White.—p. 1110.

Blood Pressure Variations in the Two Arms.—Blood pressure readings were made on both arms of 755 ambulatory patients, including some with normal and abnormal cardiovascular systems. A total of 1,388 blood pressure readings were recorded on each arm. The blood pressure was found to be higher in the right arm in 992 readings, as compared to 274 in the left arm, and to be equal in both arms in only 122 readings. The systolic variation in the two arms was 10 or more points in 694 readings. The diastolic variation was less than 10 points. Although clinically it may not be significant whether the blood pressure varies as much as 10 mm. Hg, under many circumstances even this small difference may be of vital importance to the individual. This is particularly true in examinations for life insurance, employment, or military service. It is recommended that at the first examination of any person, the blood pressure be taken in both arms, and, if no significant difference is present, that the same arm be used for follow-up studies.

Oculo-Oro-Genital Syndrome: A Deficiency Disease.—The polyhypovitaminosis accompanying protracted dietary restriction during more than three years of internment in Japanese prisoner of war camps caused much confusion to the medical officers who attempted to diagnose specific deficiency diseases. Of the various combinations of signs and symptoms one differentiated syndrome has been called the Oculo-Oro-Genital syndrome. When the first cases of trichophytosis was thought of, but stomatitis appeared in the same organismized as a deficiency disease.

pellagra. In the following few weeks more than 75% of the 8,000 American prisoners developed some degree of scrotal dermatitis, and 100 moderately advanced cases were selected for study. Within a few days of the appearance of scrotal dermatitis, glossitis developed in all of the selected group. Its first manifestations were erythema and soreness of the tip of the tongue. The tongue became very sensitive to hot or highly seasoned food. Angular stomatitis developed in 80 of the selected patients, and 17 had striated mucous patches on the inner surfaces of the cheeks. Erythema of the pharynx and soft palate was seen in 59 cases. Crops of small sensitive ulcers appeared on the buccal membranes in 32 cases. Mild to severe conjunctivitis developed in 93% of the cases, and keratitis was present in some degree in 15 cases. The syndrome was improved by two months of adequate diet. When the patients returned to an inadequate rice diet, the syndrome was far less prevalent, indicating some adaptation of the body to lowered caloric and vitamin intake. The vitamin requirements of the body appeared to be less after a loss of considerable body weight. The syndrome did not develop with a minimal diet of corn and soy beans. The syndrome is thought to be closely associated with pellagra, but is not pellagra per se.

Coccidioidal Meningitis.—One of the aims in reporting these four cases of coccidioidal meningitis was to stress the chronicity of this form of meningitis. The first patient had had a cavitary pulmonary lesion, which was followed three years later by coccidioidal meningitis. Serologic studies for coccidioidal infection suggested a disseminated form of the disease. He failed to respond to streptomycin, penicillin, and potassium iodide therapy. He was given "actidione" (an antibiotic derived from *Streptomyces griseus*) intravenously, following which he showed a remarkable clinical response and was alive three years after he was first found to have meningitis. In the second patient meningitis developed while he was stationed at a camp in California, and three years later the meningitis was still present. Therapy for 15 months, including two courses of "actidione," produced no significant change, and death finally resulted from the obstructive complications of basilar meningitis. At necropsy viable *Coccidioides immitis* were present. In the third patient the onset of illness due to *C. immitis* was never accurately determined, although during the two years preceding the appearance of the disseminated form of the disease he had had respiratory tract infections with fever while living in southern California. Involvement of the meninges was demonstrated and while he was under observation further hematogenous dissemination occurred, as illustrated by the appearance of miliary pulmonary infiltration and the necropsy findings. The original infection in the fourth patient was a relatively mild chest cold while he was working in West Texas. It was followed almost immediately by meningitis, which became chronic and did not respond to therapy. The diagnosis was made by finding the etiologic agent, *C. immitis*, at necropsy. The importance of considering coccidioidomycosis in the diagnosis of chronic meningitis is stressed.

Connecticut State Medical Journal, Hartford

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- Early Diagnosis of Tumors of Genito-Urinary Organs. A. L. Dean.—p. 959.
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A 39 Year Follow Up of Typhoid Fever Epidemic in Torrington, Connecticut. J. Lieben.—p. 983.
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Journal of Nutrition, Philadelphia

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*Effect of Frying Bacon on Nutritive Value of Protein. B. H. McBride, B. T. Guthneck, E. Hoffert and others.—p. 393.
Utilization of Dietary Calcium by Growing Albino Rats Fed Diets Containing Lard or Cocoa Butter. J. R. Beadles, H. H. Mitchel and T. Hamilton.—p. 399.
Effect of Level of Intake on Calcium and Phosphorus Metabolism in College Women. J. M. Leichsenring, L. M. Norris, S. A. Lamison and others.—p. 407.
Plasma Vitamin A and Carotene Determinations in Group of Negro Children. B. B. Szymanski and B. B. Longwell.—p. 431.
West Indian and New Orleans Negro Metabolism Tests. D. P. Qui.—p. 443.

Frying and Nutritive Value of Bacon.—To determine whether the nutritive value of protein in bacon is influenced by the frying process, McBride and associates fed lyophilized and ether extracted bacon as the sole source of protein at a 10% level to weanling rats. No reduction in the utilization of the protein by weanling rats was observed in three tests with crisp-fried (medium-done) bacon or in one test with limp-fried (medium-done) bacon as compared to control groups receiving uncooked bacon. A small statistically significant reduction in the nutritive value of the protein was observed in one test with crisp-fried bacon.

Journal of Urology, Baltimore

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*Electrolyte Disturbance in Ureterocolostomy. M. Korenberg.—p. 681.
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Interstitial Cell Tumor of Testis. H. Grabstald, J. S. Haines and J. Morrow.—p. 708.
Bilateral Interstitial Cell Tumor of Testicle. F. K. Garvey and J. Daniel.—p. 713.
Influence of Hypnosis on Semen. E. J. Farris, M. Garrison Jr. and H. Heintz.—p. 720.
Preliminary Report on Use of Tetrazolium Chloride in Genito-Urinary Cancer. R. G. Bunge.—p. 722.

Electrolyte Disturbance in Ureterocolostomy.—Recent experience with cases of bilateral ureterocolostomy with resultant changes in electrolyte structure prompted the author to study changes in electrolyte balance attributable primarily to reabsorption of sodium chloride with secondary intra and extracellular electrolyte readjustment. All patients complained of a persistently salty taste and thirst associated with ingestion of excessive amounts of water, leading to polyuria that appeared as diuresis followed by fatigue, weakness, anorexia, nausea, and vomiting. The serum sodium concentration was found to be normal or slightly elevated, the blood chloride level elevated, and the serum potassium level below normal. Injection of desoxycorticosterone administration of sodium chloride solution, and performance of bilateral ureterocolostomy all tend to cause sodium chloride retention in the body. The sodium chloride that appears in the urine of these patients is partially reabsorbed by the bowel. Reabsorption precipitates cellular dehydration with increased potassium loss from the cells and increased urinary potassium excretion.

excretion. The diarrhea tends to accentuate this potassium loss. Treatment of the disturbance must be directed at (1) inhibition of reabsorption of excess sodium chloride by encouraging the patient to empty the bowel as frequently as possible; (2) maintenance of a low sodium intake; and (3) administration of potassium salts to combat the excessive loss incurred by the frequent emptying of the bowel.

Maine Medical Association Journal, Portland

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- Management of Endometrial Carcinoma. J. A. James.—p. 327.
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Military Surgeon, Washington, D. C.

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*Exchange Resin Diuresis in Cirrhotic Ascites: Preliminary Report. G. McHardy, D. C. Browne, R. McHardy and S. Ward.—p. 187.
Management of Early Cirrhosis of Liver. W. D. Davis Jr.—p. 192.
Insomnia. T. L. Young.—p. 195.
The Psychopathic Personality in Treatment. A. T. Butterworth.—p. 197.
Present Concept of Cataract Surgery. G. M. Haik and W. Lyda.—p. 200.

Exchange Resin Diuresis in Cirrhotic Ascites.—McHardy and associates used resin therapy in 28 patients with edema and ascites associated with hepatic disease. Three patients were not benefited, but resin controlled fluid retention in the remaining 25 patients without appreciable complications. Ammonium resin, by diminishing sodium and potassium absorption from the intestine through fixation and fecal excretion, reduces their respective serum levels and their urinary excretion. Any method of managing ascites is more desirable than paracentesis in control of cirrhosis of the liver, because of the great protein loss caused by paracentesis in a disease characterized by hypoproteinemia. Resin acidosis produced by concomitant ammonium chloride absorption and diminished base absorption probably potentiates mercurial diuresis. The irritation caused by increased urinary ammonium chloride excretion possibly explains the cylindruria common to the use of resins. Hypokalemia may be produced by ammonium cation resin. In the early stages of this study an ammonium potassium resin was not available. At present most patients are receiving this resin, which theoretically prevents hypokalemia. In addition the newer preparations are more palatable, being of finer mesh. Since the use of resin had an unfavorable effect in a case of renal impairment, the authors feel that resins should not be used in the presence of renal insufficiency. They conclude that resins will probably prove valuable adjuncts to the management of sodium retention edema in carefully supervised cases. Laboratory studies essential for the guidance to resin therapy require flame photometric studies. These are expensive and limit the use of resins in general practice.

North Carolina Medical Journal, Winston-Salem

12:525-572 (Nov.) 1951

- Iatrogenic Diseases. W. M. Nicholson.—p. 525.
Preliminary Report on Follow-Up of Prefrontal Lobotomies Performed by the Duke Neurosurgical Staff. L. B. Hohman, G. L. Odom, R. B. Suitt and others.—p. 529.
Psychosomatic Medicine. J. D. Bradley.—p. 534.
Pediatrics in General Practice. J. R. Bender.—p. 539.
Clinical Evaluation of 1-(B-Dimethylaminoethoxy)-3-n-Butylisoquinoline Monohydrochloride as an Antipruritic Agent. J. L. Callaway, W. T. Watkins Jr., G. W. Crane Jr. and S. C. Dees.—p. 546.
Clinical Appraisal of New Antipruritic (N-ethyl-o-crotonotoluide). J. M. Hitch.—p. 548.
Eugenic Sterilization in North Carolina. C. J. Gamble.—p. 550.

Proc. Soc. Exper. Biol. & Med., Utica, N. Y.

78:1-362 (Oct.) 1951. Partial Index

- Distribution of Radioactive Phosphorus in Normal and Diseased Brain Tissue: Experimental and Clinical Observations. W. E. Stern and C. Marshall.—p. 16.
Potentiating Effect of ACTH and of Cortisone on Pressor Response to Intravenous Infusion of L-Nor-Epinephrine. G. S. Kurland and A. S. Freedberg.—p. 28.
Differences in Cellular Pathogenicity of Two Immunologically Related Poliomyelitis Viruses as Revealed in Tissue Culture. N. Ledinko, J. T. Riordan and J. L. Melnick.—p. 83.
Effect of Cortisone, Related Hormones, and Adrenalectomy on Susceptibility of Mice to Virus Infections. C. M. Southam and V. I. Babcock.—p. 105.
Intravenous Treatment of Pernicious Anemia with Citrovorum Factor (Leucovorin). L. M. Meyer, W. C. L. Diefenbach and C. M. Brahner.—p. 119.
Effect of Intravenous Aureomycin on Intestinal Flora of Dog and Man. S. Jacob, F. B. Schweinburg and A. M. Rutenburg.—p. 121.
Placental Transmission of Mumps and Streptococcus MG Antibodies. A. L. Florman, B. Schick and H. E. Scalettar.—p. 126.
Microwave Diathermy Treatment of Frostbite. R. B. Lewis.—p. 163.
Chloromycetin Palmitate: Its Use in Pediatrics. V. DeP. Larkin.—p. 191.
System for Measuring and Designating Antigenic Components of Influenza Viruses with Analyses of Recently Isolated Strains. M. R. Hilleman.—p. 208.
*Effect of Early Small Exchange Transfusion on X-Irradiated Dog. S. N. Swisher and F. W. Furth.—p. 226.
*Megaloblastic Anemia in Pregnancy: Remission Following Combined Therapy with Ascorbic Acid and Vitamin B₁₂. R. G. Holly.—p. 238.
Evidence for Sodium Retaining Factor in Toxemia of Pregnancy. J. J. Chart, E. G. Shipley and E. S. Gordon.—p. 244.
Changes in Adrenal and Pituitary Concentrations of I¹³¹ and P³² Following Thyroidectomy. J. B. Boatman, J. H. Sunder, C. Russ and C. Moses.—p. 250.
Simultaneous Occurrence of Two Immunological Types of Group A "Coxsackie" Virus in Case of Herpangina. E. A. Beeman, R. H. Parrott and R. M. Cole.—p. 295.
Central Nervous Depressive Effect of Khellin. G. Chen, C. R. Ensor and D. Russell.—p. 305.
Complement-Fixing Murine Typhus Antibodies in Vitamin Deficiency States: II. Pyridoxine, and Nicotinic Acid Deficiencies. K. Wertman and J. L. Sarandria.—p. 332.
Effect of ACTH upon Gastric Secretion. S. J. Gray, J. A. Benson Jr. and R. W. Reifstein.—p. 338.
Mechanisms of Amethopterin Resistance in Leukemia: I. Effects of Weak Folic Acid Antagonists on Mouse Leukemias. J. H. Burchenal, S. F. Johnston and G. B. Waring.—p. 348.

Effect of Exchange Transfusion on Irradiated Dogs.—Immediate removal of 250 cc. of blood and replacement with an equal volume of normal compatible whole blood in 20 lb. (9.1 kg.) dogs given 440 r whole body irradiation (expected LD 80) resulted in a marked delay in onset of radiation syndrome and mortality. There was a suggestive decrease in ultimate mortality as well. The authors feel that these findings suggest the feasibility of attempting immediately after exposure relatively large exchange transfusion of fresh blood in humans exposed to doses of whole body irradiation in the range of high lethality, such as might occur with an accidental laboratory exposure.

Megaloblastic Anemia in Pregnancy: Response to Ascorbic Acid and Vitamin B₁₂.—After citing reports indicating the lack of response to vitamin B₁₂ of megaloblastic anemia of pregnancy, Holly reports the history of five patients with this type of anemia. The relation of this anemia to ascorbic acid deficiency suggested by the effectiveness of combined ascorbic acid and vitamin B₁₂ therapy when vitamin B₁₂ alone was given. The patients did not respond to adequate doses of vitamin B₁₂ alone. These patients later had a complete response when ascorbic acid was added to the therapy. The authors

to folic acid therapy and blood transfusions. Two patients were treated for short periods of time with ascorbic acid alone. A minimal response in reticulocytes was observed in one. Subsequent additions of vitamin B₁₂ to the therapy after saturation with ascorbic acid produced a complete hematologic remission. One patient had a spontaneous remission after delivery. In three patients combined therapy with ascorbic acid and vitamin B₁₂ produced a complete remission.

Public Health Reports, Washington, D. C.

66:1451-1486 (Nov. 9) 1951. Partial Index

- Plague on the High Seas. V. B. Link.—p. 1466.
Q Fever in California: IV. Occurrence of *Coxiella Burnetii* in Placenta of Naturally Infected Sheep. H. H. Welsh, E. H. Lennette, F. R. Abinanti and J. F. Winn.—p. 1473.
Salmonella Mendoza: New Salmonella Type. R. H. Leiguarda, O. A. Peso, A. Z. R. de Pelazzolo and E. M. Ansiaume.—p. 1478.

66:1487-1522 (Nov. 16) 1951

- Trends and Epidemics of Influenza and Pneumonia, 1918-1951. S. D. Collins and J. Lehmann.—p. 1487.

South Dakota J. Med. & Pharmacy, Sioux Falls

4:295-316 (Nov.) 1951

- *Rationale and Technique of Sex Hormone Replacement in the Aged Female: Preliminary Result Report. W. H. Masters.—p. 296.

Sex Hormone Replacement in Aged Women.—Sex hormone replacement in women to avoid the results of metabolic imbalances associated with the menopause has been recommended by some clinicians, while others have warned against it because the sex steroids may be carcinogenic. Experiments were instituted on aged female patients (65 to 85 years) at the St. Louis City Infirmary. Bedridden as well as physically active patients were selected, and women with diabetes, essential hypertension, or advanced arthritis were included. Patients were first given a complete physical and laboratory examination. Estradiol benzoate was administered in cycles until withdrawal bleeding could be obtained. Then the patients were treated by one of the following methods: (1) cyclic estrogen exhibition and withdrawal at regular intervals to shed the endometrium; (2) constant estrogen influence with cyclic progesterone exhibition and withdrawal to shed the endometrium; (3) constant estrogen influence with cyclic testosterone exhibition and withdrawal to shed the endometrium; and (4) constant estrogen influence and testosterone opposition to such a degree that hyperplasia is avoided and shedding of the endometrium unnecessary. All patients were subjected to repeated physical and laboratory check-ups while under therapy. There was a generalized physical and mental improvement in many of the patients under long continued therapy. Occasionally improvement was startling. The investigators cannot explain clinical improvement on the basis of laboratory findings, as results of most tests were consistently negative. Early autopsy findings suggest important changes in the vessel walls of target organs.

Urologic & Cutaneous Review, West Palm Beach, Fla.

55:649-714 (Nov.) 1951. Partial Index

- Pneumopyelography. J. S. Ritter and W. H. Shehadi.—p. 649.
*Genital Edema in Carcinoma of Prostate. C. R. O'Crowley and A. R. Fernicola.—p. 652.
Androgenic Adenoma of Adrenal Gland. S. F. Wilhelm and L. Kamens.—p. 659.
Plastic Operation for Benign Lesions of Urethral Meatus. L. C. Scheffey and W. R. Lang.—p. 665.
Normal Intravenous Pyelograms in Presence of Hydronephrosis. C. Ney.—p. 667.
Hemangioma of Kidney: Review of Literature. L. E. McCrea.—p. 670.
*Calcification of Renal Artery Manifested by Gastro-Intestinal Tract Symptoms. J. C. Kimbrough.—p. 680.

Genital Edema in Carcinoma of Prostate.—The patient described had atypical features of carcinoma of the prostate, with massive edema of the penis and scrotum as an initial sign; greatly enlarged inguinal lymph nodes; a normal sized, soft, movable prostate gland with no induration; perirectal lymph nodes found on rectal palpation; low grade fever; and a fulminating course. The authors conclude that edema of the penis

and scrotum with inguinal lymphadenopathy may at times be the only clinical manifestation of carcinoma of the prostate, and that far-advanced, retrograde lymphatic carcinomatosis can occur in the absence of urinary symptoms, pain, induration of the prostate, and osseous metastases. The so-called soft carcinoma apparently lacks the fibrous tissue responsible for hardness. An explanation is that the soft prostate is more cellular and that in these cases the cellular activity is more accelerated than the response of the fibromuscular stroma. It may be that intra-acinar rather than extra-acinar malignant cell growth occurs, that it does not induce a fibrous tissue reaction, and that it advances more rapidly in the tubules than in the stroma. When pelvic lymph nodes are palpable per rectum in the absence of induration of the prostate and seminal vesicles, the serum acid phosphatase should be determined to aid the diagnosis.

Gastrointestinal Symptoms in Renal Disease.—Kimbrough reports the case of a woman, aged 47, whose illness began with pain in the upper part of the abdomen, indigestion, flatulence, and general abdominal discomfort. The patient was treated for gallbladder and gastrointestinal disease. When the symptoms persisted, a thorough examination of the liver, gallbladder, gastrointestinal tract, and cardiovascular system was made, but no abnormality was found. X-ray examination revealed a density in the region of the upper pole of the right kidney and a tubular density near the same kidney, and a urological examination was made. Excretory and retrograde urograms showed moderate hydronephrosis and nephroptosis of the right kidney. At operation a calculus 1 cm. in diameter was found in the upper right calix. The right kidney was removed. Recovery was uneventful, and the symptoms were completely relieved. Pathologic studies disclosed a calcified artery at the hilus. The author states that the literature contains many reports of renal disease manifested by gastrointestinal symptoms, yet patients with renal disease are often treated many months for liver, gallbladder, and gastrointestinal tract disease before a complete urological examination is done.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

59:551-602 (Nov.) 1951

- Some Factors Concerned with Liver Injury. I. S. Ravdin.—p. 551.
Intramedullary Nailing of Ulna in Fractures of Both Bones of Forearm in Adults. C. E. Anderson.—p. 559.
Management of Vaginal Bleeding During Last Trimester of Pregnancy. R. E. Crowder, E. S. Bills and J. B. Claire.—p. 565.
Points of Perineal Repair Technic. A. P. Hudgins.—p. 570.
Surgical Problems in the Aged. M. W. Durham.—p. 574.
*Surgical Repair of Esophageal Hiatus Hernia: Modification in Technic. C. E. Rees.—p. 579.
Surgical Extirpation of Tuberculous Psoas Abscess: Preliminary Report on Six Cases. J. A. Weinberg.—p. 584.
Experimental Studies on Circulation to Liver in Relation to Protocaval Anastomosis. R. Cohn and J. Connelly.—p. 589.

Surgical Repair of Esophageal Hiatus Hernia.—From 1940 to 1950 a total of 212 cases of esophageal hiatus hernia were detected roentgenologically at this clinic. In 15 surgical repair was done. The remaining 197 patients were treated by dietetic and general medical means. Patients receiving medical treatment because the hernia is small and the symptoms slight should be kept under observation, since herniation tends to be progressive. The symptoms of hiatus hernia may simulate those of coronary disease, gastric and duodenal ulcer, gallbladder disease, and functional digestive syndromes. It is, therefore, imperative that these patients be studied completely and carefully so that, when surgical repair is recommended, the surgeon can be reasonably certain that the hiatus hernia is the source of the symptoms. Surgical repair is recommended if symptoms are distressing, hemorrhage occurs, or bleeding is continual. Of the 15 patients operated on by the author, repair was done in three by the transabdominal route and in 12 by the transthoracic route. Reasons are given for favoring the latter approach. There were no deaths, but one recurrence in each group. A surgical modification is described, wherein the diaphragm is incised and the upper end of the greater curvature of the stomach is sutured to the under surface of the diaphragm to keep the stomach and lower end of the esophagus in the abdomen while adhesion of the esophagus to the hiatal margin is taking place.

FOREIGN

Acta Obstet. et Gynec. Scandinavica, Stockholm

31:1-108 (No. 1) 1951. Partial Index

- Interlocked Twins: Report of Two Cases. B. Stenström.—p. 1.
 Climacteric Following Supravaginal Hysterectomy. K. Knutsen.—p. 9.
 •Early Ambulation Following Delivery. H. Zilliacus.—p. 25.
 Level of Diastase and Sugar in Blood of Nursing Women. J. A. Abolins.—p. 39.
 Jaundice During Pregnancy. M. Ingerslev and G. Teilmann.—p. 74.
 Small-Cystic Degeneration of Ovaries as Incidental Finding in Gynecological Laparotomies. P. Vara and K. Niemineva.—p. 94.

Early Ambulation After Delivery.—Early ambulation after delivery was recommended by Küstner in Germany in 1878 and by Ries in the United States in 1899, but both were considered heretics by their contemporaries. Since 1924 early ambulation has been urged with increasing frequency after surgical procedures, but it has not been so widely recommended after delivery. At the Women's Clinic of the University of Helsinki early ambulation after delivery has been practiced since 1939. The effect of early ambulation after delivery on the incidence of puerperal complications was studied in 12,847 women. Within eight days of delivery 10,194 patients had left the hospital; in cases in which a cesarean section had been performed, the patients left on the 10th to 14th day. There were no deaths among the patients in whom early ambulation was encouraged. The author cites statistics on the incidence of pneumonia, thrombosis, pulmonary embolism, and various other complications, and says that while it must be admitted that the effect of early ambulation with regard to displacement of the uterus is still uncertain, its many advantages outweigh a few possible disadvantages. The women in whom early ambulation was encouraged regained their general physical well-being very rapidly.

Archiv für klinische Chirurgie, Heidelberg

269:183-280 (No. 3) 1951. Partial Index

- Parasternal Diaphragmatic Hernia. M. Lüscher.—p. 183.
 Eosinophilic Infiltration of Gallbladder. G. Linzenmeier.—p. 215.
 •Limitations of Sympathectomy in Disturbances of Peripheral Blood Perfusion: Critical Evaluation of Preoperative Tests. J. Konec.—p. 223.
 •Histologic Picture and Prognosis of Carcinoma of Breast. H. Chiari.—p. 247.

Sympathectomy in Disturbances of Peripheral Circulation.—The value of a test preceding sympathectomy is most clearly shown in cases of organic circulatory disturbances, when clinically necrosis seems evident or possible and survival of an extremity is doubtful. Following critical evaluation of preoperative tests, the author discusses the possibilities of measuring the collateral circulation and the effects of a sympathectomy on blood circulation and metabolism. His explanation of the close connection between circulation and metabolism and its dependence on the sympathetic innervation make it clear that, if sympathectomy is done in unsuitable cases, a threatening impairment of the circulation or of the oxygen supply of the tissue may be intensified by the intervention on the sympathetic system. Four case histories are presented in which intervention on the sympathetic system was largely responsible for the rapid deterioration of the circulation of an extremity. The author stresses that in obliterating vascular diseases the fate of a diseased extremity depends on the condition of the collateral circulation. Information as to whether sympathectomy will improve the circulation in such cases is provided by continuous thermoelectric measurement of the skin temperature and by a test employing venous stasis. Sympathectomy produces much more than simply an increase in circulation. An increase in blood volume seems to be a secondary effect of the increased metabolic oxygen requirements resulting from abolishing metabolism-inhibiting sympathetic impulses. On the other hand, if the sympathetic tonus is increased, the metabolic oxygen requirements are less as the result of neurogenic limitation of oxidative processes. This explains the increased oxygen content of the venous blood of a diseased extremity. Thus there are cases of defective circulation in which sympathectomy not only is not helpful but may actually cause further deterioration of impaired tissue.

Histologic Picture and Prognosis of Breast Carcinoma.—Chiari discusses the histologic picture of mammary carcinoma on the basis of 1,600 surgically removed breasts. Scirrhus carcinoma was found in 603 cases, or 37.6%, among which were 391 patients with purely scirrhus and 212 with solid scirrhus carcinoma. Solid medullary carcinoma was found in 125 (7.9%) of the patients. Diffuse carcinoma, also known as carcinomatous mastitis, was observed in only 17 (1%) of the patients. Carcinoma solidum simplex was relatively frequent, accounting for a total of 581 cases (27.5%). In the 441 cases with the pure form of carcinoma simplex, cancer cells were found only in the stroma, but in the remaining 140 cases they also showed intracanalicular localization. The mammary cancer designated as carcinoma cribriform or duct carcinoma was identified in 86 (5.3%) of the cases. In this type 18 cases of the intracanalicular form, the so-called pure cases were differentiated from those with the extracanalicular form. The differentiation between "pure" and "also extracanalicular" is made in the comedo carcinomas, accounting for 5 and 25 cases, respectively. There was a total of 124 cases of adenomatous carcinoma, including 16 cases of the purely adenomatous form, 33 cases of the adenomatous papillary form, and 75 cases of the semiadenomatous form. Gelatiniform carcinoma was observed in 29 (1.8%) of the cases. Carcinoma basocellulare was seen in only five cases. Discussing the relationship between lymph node involvement and survival, the author states that in the most frequent histologic forms (scirrhus and simplex) the incidence of lymph node involvement is almost equally high (66% and 74%), and the prognosis therefore equally unfavorable. The fortunately rare diffuse carcinoma has an unfavorable prognosis, but the adenomatous forms have a relatively favorable prognosis. In the types in which intra and extracanalicular growth can be differentiated, those with extracanalicular growth generally have a higher rate of lymph node involvement, but it is not justifiable to consider the prognosis of the adenomatous carcinomas as always more favorable than for the scirrhus carcinomas, because among the former some are highly malignant.

British Journal of Ophthalmology, London

35:573-636 (Oct.) 1951. Partial Index

- Hereditary Degeneration of Mouse Retina. K. Tansley.—p. 573.
 Present Status of Physiotherapy in Ocular Disease. P. D. Trevor-Roper.—p. 583.
 Closed Branches of Conjunctival Vessels. A. Loewenstein.—p. 595.
 Trachoma: Diagnosis and Treatment. L. de Andrade.—p. 601.
 Proptosis Caused by Hydatid Disease. Ahmad Bey Handousa.—p. 607.
 Factors Affecting Penetration of Antibiotics into Aqueous Humour. M. Langham.—p. 614.
 Theoretical Considerations for Artificial Corneal Implant. O. E. E. Anderson.—p. 628.

British Medical Journal, London

2:1233-1294 (Nov. 24) 1951

- Psychiatry of Cerebral Diseases. M. Bleuler.—p. 1233.
 Social Adjustment of Neurotic Patients After Prefrontal Leucotomy. A. A. Baker and L. Minski.—p. 1239.
 Simple Gastric Ulcer and Carcinoma. B. F. Swynnerton and S. C. Truelove.—p. 1243.
 •Use of Oral Cortisone in Paediatrics. B. Wolman.—p. 1246.
 Iron Metabolism in Pregnancy. A. Klopfer and S. Ventura.—p. 1251.
 Diabetic Gangrene. A. Grunberg, H. L. Davies and J. L. Blair.—p. 1254.
 Associated Perforation and Haemorrhage in Peptic Ulcers: Treatment by Immediate Gastrectomy. N. S. Slater.—p. 1257.
 Bronchiectasis with Unsuspected Foreign Body. B. P. Moore.—p. 1259.

Oral Administration of Cortisone to Children.—Three children with rheumatoid arthritis, one child with acute rheumatic pericarditis, and one child with nephrosis were given 25 mg. tablets of cortisone acetate once, twice, or three times daily as required. The oral administration of cortisone suppressed the rheumatic process in the three children with rheumatoid arthritis and the child with rheumatic pericarditis. Diuresis was produced and a remission obtained in the patient with nephrosis. Equal amounts of cortisone given orally were as promptly and as completely effective as cortisone given parenterally as long as the daily dose was given in divided amounts or three times a day.

Canadian Medical Association Journal, Montreal

65:523-622 (Dec.) 1951

- Aspects of Anaesthesia. H. R. Griffith.—p. 523.
 Accidents in Children. C. Collins-Williams.—p. 531.
 Studies on Poliomyelitis in Ontario: V. Further Observations on Recovery of Coxsackie Viruses from Cases of Clinical Poliomyelitis. N. Silverthorne, C. Anglin, J. B. J. McKendry and others.—p. 536.
 Decline of Artificial Pneumothorax. W. B. Phair.—p. 542.
 Leukaemia in Children. C. L. Rodgers, W. L. Donohue and C. E. Snelling.—p. 548.
 *ACTH and Cortisone in Treatment of Acute Leukaemia. D. G. Cameron, S. R. Townsend, E. S. Mills and W. H. Mathews.—p. 552.
 Folic Acid and Antagonists in Treatment of Leukaemia in Children. B. Laski, J. M. M. Darte, C. E. Snelling and W. L. Donohue.—p. 556.
 *ACTH and Cortisone in Treatment of Leukaemia in Children. J. M. M. Darte, C. E. Snelling, B. Laski and others.—p. 560.
 ACTH and Cortisone in Treatment of Pemphigus Erythematosus. J. Mallek, B. Kanee and J. Zack.—p. 564.
 Phosphorus Sesquisulphide Poisoning. J. F. Burgess.—p. 567.
 Radiologist and Epigastric Pain. A. E. Broome.—p. 569.
 Schistosome Dermatitis in Quebec. M. J. Miller and E. Monroe.—p. 571.
 Laryngeal Swab Specimen in Cultural Diagnosis of Pulmonary Tuberculosis. A. R. Armstrong.—p. 575.
 Conservative Treatment of Sinusitis. G. E. Tremble.—p. 578.
 Studies on Fungistatic Powers of New Benzothiazol and Antihistaminic Compound. E. E. Seale.—p. 582.

Corticotropin and Cortisone in Acute Leukemia.—The observation that increased function of the adrenal cortex in animals causes involution of normal lymphoid tissues, that administration of compound E causes regression of a lymphoid tumor in mice, and that alterations in adrenal cortical function occur in patients with lymphoid neoplasms suggested that administration of cortisone or corticotropin (ACTH) might influence favorably the course of acute leukemia in man. Nine patients with acute leukemia were treated with corticotropin or cortisone at the Montreal General Hospital from December, 1949, to December, 1950. Despite this treatment all had died by June, 1951. Five of the patients died within a month, three others in less than six months, and the longest survivor lived for only nine months from the onset of the disease. It is concluded that corticotropin and cortisone were of little practical value in the treatment of these nine cases of acute leukemia, although clinical improvement occurred in each of the 9 patients while hormone therapy was being given.

Corticotropin and Cortisone in Leukemia in Children.—In all, 7 children with leukemia were treated with corticotropin (ACTH) and/or cortisone. There were 20 boys and 17 girls from 15 months to 14 years of age. In all cases the history and clinical condition at the time of first admission indicated that the expected survival time without treatment would have been less than one year. Periods of treatment that resulted in complete remission varied from 15 to 35 days. Temporary remissions occurred in approximately 50% of the patients, but none could be considered as cured or permanently benefited. Although repeated remissions were obtained in a few children, all eventually became refractory to further hormone therapy. The authors feel that corticotropin and cortisone, although unsatisfactory for the permanent treatment of leukemia in children, are valuable in the further investigation of this disease.

Cardiologia, Basel

18:321-376 (No. 6) 1951

- The Electrocardiogram in Acute Poliomyelitis. P. F. Reubi and G. Bornstein.—p. 321.
 Constitutional Changes in Patients with Coarctation of the Aorta. P. I. Halonen, P. E. Heikel and P. Majanen.—p. 333.
 Quantitative Representation of Given Vectors in the Unipolar and Bipolar Extremity Leads and the Goldberger Leads. V. H. Gillmann.—p. 339.
 Electrophysiologic Investigations on the Starling Heart-Lung Preparation. V. W. Brendel, H. Gladewitz, F. Hildebrandt and W. Trautwein.—p. 345.
 *Acute Non-Specific Myocarditis in Scarlet Fever and Acute Hemolytic Tonsillitis: Clinical Investigation of 3,069 Cases of Scarlet Fever, 798 Cases of Acute Tonsillitis, and 33 Cases of Hemolytic Streptococcus Carriers. E. Bengtsson, G. Birke and H. Wingstrand.—p. 360.

Myocarditis in Streptococcal Infections.—Acute nonspecific myocarditis was found in 3.9% of 3,069 cases of scarlet fever and in 4.4% of 798 cases of acute tonsillitis due to hemolytic streptococci. Among the adults in the group the incidence of myocarditis was 9% in scarlet fever and 9.4% in tonsillitis.

Among the children the corresponding figures were 3.7% and 2.8%. No case of myocarditis was found in 333 carriers of hemolytic streptococci. Myocarditis appeared during the first week of illness in about half the cases, but lasted only a few weeks in the majority. Convalescence was slower in patients with myocarditis than in those with uncomplicated infections. The diagnosis of myocarditis was based on the presence of electrocardiographic changes, usually accompanied by tachycardia and often by transient murmurs, increased antistreptolysin titers, and greatly increased sedimentation rates. Electrocardiographic changes occurred chiefly in the ventricular complex. T wave changes were the only abnormality in the tracings of 60% to 65% of these patients. The authors believe that greater attention should be given to the cardiac complications of acute tonsillitis. While in their series myocarditis had an innocuous course they believe that in some cases it may lead to hypertrophy of the heart and scar formation. In adults it persisted longer and had more pronounced effects than in children.

Deutsche medizinische Wochenschrift, Stuttgart

76:1421-1484 (Nov. 16) 1951. Partial Index

- Myocardosis, Endocardosis and Cardiosclerosis. F. Lange.—p. 1421.
 *Chemotherapy and Tamponade of Lung Cavities. G. Maurer.—p. 1423.
 Bone Marrow Atrophy and Bone Marrow Fibrosis. R. Stodtmeister and S. Sandkühler.—p. 1431.
 *Pathogenesis, Diagnosis and Treatment of Acute Pancreatic Necrosis. H. Wildegans.—p. 1458.

Chemotherapy and Tamponade of Lung Cavities.—The proposed modification of surgical treatment of large lung cavities has three phases as follows: Cavernostomy is the preparatory phase by which a canal is created between the skin and the cavity wall, i. e., a stoma that may be enlarged gradually with dechloridated Laminaria packing. This is followed by the main phase of treatment by tamponade of the disintegrating cavity with gauze strips soaked with a 5% solution of *p*-aminosalicylic acid, to which 250 units of penicillin per cubic centimeter had been added. Instillation of the chemotherapeutic solution may be repeated with an olive-pointed sound at two hour intervals. Simultaneously 3 to 5 tablets (150 to 250 mg.) of ethyl-ureide-benzal-thiosemicarbazone ("tebazy") should be given daily by mouth. Intracavitary injections of streptomycin may be reserved for patients with toxic manifestations due to thiosemicarbazone, or may be used as additional treatment for intercurrent disseminations. After the cavity has become sterile and shrunk and tuberculous foci may no longer be demonstrated on endoscopy closure of the draining bronchi should be attempted by production of an eschar with the aid of high frequency electric current or other measures. The stoma may close spontaneously in from several days to four weeks after this final phase of the treatment, and a small funnel-shaped cutaneous scar remains. To prevent complications the pleural cavity must be completely obliterated; artificial pleural synechia may be obtained occasionally with repeated kaolin injections. In addition the vital capacity must be determined, and the lower limit of 1,300 cc. should never be exceeded. Seven cases are reported that show that the sputum of the patients with cavernous breakdown may become negative within two months after the tamponade with chemotherapy. Because of sterilization of the disintegrating cavity the occurrence of bronchial fistula, the most frequent and dangerous risk associated with lobectomy and pneumonectomy, may be prevented. The method is particularly recommended for treatment of tuberculous cavities in aged patients and is of vital importance for mother and child when performed in tuberculous women before conception or during pregnancy.

Acute Pancreatic Necrosis.—Of 205 patients with acute pancreatic necrosis, 144 (70%) were women and 61 (30%) were men. After a sudden decrease in the incidence of acute pancreatic necrosis in Germany during the hunger years 1945-1946 the incidence increased as nutrition improved. The bile ducts are a significant part in the pathogenesis of this disease; of the 205 patients with acute pancreatic necrosis, 187 (91%) had cholelithiasis and cholecystitis, and 14 (7%) had choledocholithiasis. According to the canalicular concept of the pathogenesis of acute pancreatic necrosis, the bilipancreatic reflux activated trypsin, but the author considers this explanation unsatisfactory. The formation of large sequestrums in the pancreas suggests

that the blood supply has been disturbed (vascular concept). In three fatal cases of acute pancreatic necrosis necropsy revealed processes of the endarteritis obliterans type. The significance of the functional neuromuscular and neurovascular factor is emphasized. Acute and chronic involvement of the pancreas frequently may result from biliary colic, but the classic picture of acute pancreatic necrosis may not be observed. The author's clinical observations did not confirm that an allergic-hyperergic reaction is a factor in the disease, but endocrine influences may play a decisive part. Pancreatic edema is not to be considered a variety of acute pancreatic necrosis, but is a preliminary phase of the disease. Determinations of pancreatic ferments and tests of endocrine pancreatic function (hyperglycemia, amylosuria, lipasemia, hypoprothrombinemia, and hypocalcemia) are of considerable aid in establishing a tentative diagnosis. Of the 205 patients, 22 with doubtful diagnosis were subjected to laparotomy while surgical treatment was delayed for 183 patients with established diagnosis. Of 66 patients who after three to six weeks of conservative treatment were subjected to secondary cholecystectomy and drainage of the common bile duct, 59 made a complete recovery. The presence of an intrapancreatic or parapancreatic abscess necessitates drainage as soon as possible.

Hospital, Rio de Janeiro

5:665-842 (Nov.) 1951. Partial Index

*Fetal Opisthotonos in Face Presentation. O. Sandoval.—p. 697.

Opisthotonos in Face Presentation.—Delivery of the child in face presentation is a rare cause of opisthotonos in the newborn, but intracranial hemorrhage, meningitis, tetanus, tetania (hypoparathyroidism), hydrocephaly, and kernicterus are more frequent causes. In face presentation, opisthotonos is due to sustained strong contraction of the dorsal muscles of the child in the uterus with consequent extreme hyperextension of the child's back during delivery. In the Maternity Hospital of the National Faculty of Medicine of the University of Brazil, of a total of 7,222 deliveries observed in four years, 13 were face presentations. This is 1 infant born in face presentation for every 555 deliveries. In face presentation the membranes are ruptured early. Delivery of the child is delayed two to four hours in comparison with normal delivery. In most cases a cesarean section is indicated. The face of the newborn shows edema of the lips, cheeks, and eyelids. A mucoserous secretion is eliminated from the mouth and eyes. Sometimes the infant cannot take the breast for the first few days after birth. There are minute subconjunctival hemorrhages. The thyroid is swollen. In cases of opisthotonos the head remains in extreme extension about a week and then spontaneously returns to normal position after the face has become normal. Intracranial hemorrhage or meningitis may be diagnosed as the cause of the opisthotonos. This condition has been reported in the literature only in two cases. It occurred in one of the 13 cases of face presentation observed by the author.

Lancet, London

2:947-996 (Nov. 24) 1951

- Mechanics of Voluntary Muscle. A. V. Hill.—p. 947.
- *Primary Partial Gastrectomy for Perforated Ulcer. J. F. Nuboer.—p. 952.
- Differences in Behaviour of Sensitized Red Cells to Agglutination by Antiglobulin Sera. J. V. Dacie.—p. 954.
- Demonstration of Multiple Antibodies in Antiglobulin Sera. H. Crawford and P. L. Mollison.—p. 955.
- *Evolution of Toxic Thyroid Gland: Clinical and Pathological Study Based on 2,114 Thyroidectomies. T. Levitt.—p. 957.
- Use of Depressant and Relaxant Drugs in Infants and Children. S. M. Anderson.—p. 965.
- Adrenaline and Noradrenaline Concentrations in Adrenal Glands at Different Ages and in Some Diseases. G. B. West, D. M. Shepherd and R. B. Hunter.—p. 966.
- Aluminium Foil on Operation Wounds. W. F. W. Southwood.—p. 969.
- Nerve Nipping at Intercostal Margin. F. H. Stevenson.—p. 969.

Primary Partial Gastrectomy for Perforated Ulcer.—Nuboer says that in Holland partial gastrectomy was first recommended for perforated ulcer in 1933. At first it was performed only on young patients, and preferably within six hours of perforation. Favorable results led to broadening of the indications; and since 1943 partial gastrectomy has been done in nearly all cases of

perforated ulcer at the Utrecht University Hospital. Of a total of 212 patients with perforated ulcer treated at this hospital in the last 11 years, 131 were subjected to primary partial gastrectomy. Most of the patients were operated on within nine hours of the perforation by the Polya modification of the Billroth II method. Five or 3.8% of the patients died, three of peritonitis, one under the anesthetic, and one as the result of an injury to the biliary and pancreatic ducts. As the primary mortality is lower than that attained with simple suture of the perforation or with conservative treatment, and as the late results also surpass those obtained with the other two methods of treatment, the author feels that partial gastrectomy should be adopted as the standard treatment for perforated peptic ulcer.

Evolution of Toxic Thyroid Gland.—Hitherto it has been widely accepted that the various diseases of the thyroid bear little if any relation to one another. However, a close study of 2,114 consecutive patients who underwent thyroidectomy has led Levitt to believe that these apparently separate conditions are actually successive stages in a single disease of the thyroid. Pathologically 706 thyroids were typical of epithelial hyperplasia, and 704 were examples of the lymphoid phases of the toxic thyroid gland. It is suggested that the toxic thyroid gland evolves from the epithelial hyperplasia characteristic of classical Graves' disease, through successive phases of lymphoepithelial hyperplasia, focal and then diffuse lymphoid hyperplasia, and fibrolymphoid hyperplasia, to the final stage of fibrosis. The microscopic, macroscopic, and clinical features of these stages are defined and analyzed. The patients' age, the degree of toxicity, exophthalmos, lid retraction, recurrence rate, preoperative, and postoperative weights, and the incidence of postoperative hypothyroidism all show a transition that closely corresponds to the pathological phases of the thyroid gland. In succeeding phases the epithelial elements of the degenerating toxic thyroid gland diminish. The lymphoid tissue waxes and then wanes. The final state of irreversible fibrosis terminates this process. The degenerated and atrophied epithelial cells are steadily buried by masses of lymphoid tissue. These islets of epithelial cells may flare up into intense regenerative hyperplasia, with short-lived toxicity, and then revert to a state of myxedema. In the final phase of fibrosis the many extraglandular adhesions make simple thyroidectomy a hazardous procedure. The more lymphoid or fibrous its constituents, the less toxic does the gland become, thereby diminishing or eliminating the need for preoperative antithyroid drugs. The more epithelial elements present, the smaller should be the thyroid residue left at operation, and the greater is the need for ligation of the inferior thyroid arteries. Persistent or recurrent thyrotoxicosis of epithelial hyperplasia may necessitate another operation or use of radioactive iodine. Subsequent hypothyroidism in the phase of lymphoid hyperplasia and the development of myxedema in the fibrolymphoid phases must be treated by thyroid substitution therapy.

Maandschrift voor Kindergeneeskunde, Leyden

19:407-422 (Nov.) 1951

- Blood Coagulation and Blood Proteins. E. Gorter.—p. 407.
- *Four Years' Experience in Treatment of Tuberculous Meningitis. C. Hooft and V. Deneve.—p. 423.

Treatment of Tuberculous Meningitis.—Of 143 children with tuberculous meningitis who were treated between May, 1947, and January, 1951, 21 died within three days of admission. In July, 1951, 63 or nearly half of the remaining 122 were living. The authors gained the impression that the intramuscular injection of *p*-aminosalicylic acid must be continued uninterruptedly for at least six months, the daily dose for infants being 500 mg. and for older children up to 1 gm. Treatment with streptomycin should be gradually discontinued after six months. For the intrathecal administration of streptomycin, small doses should be used (25 to 50 mg.), and they should not be given too often. When the protein index of the cerebrospinal fluid rises, frequent punctures are indicated, but without injection of streptomycin. With this treatment 23 of 32 patients over two years old survived. Unfavorable prognostic factors are low age, late diagnosis, and sensory disturbances on admission.

Medical Journal of Australia, Sydney

2:517-548 (Oct. 20) 1951

- *Congenital Pulmonary Valvular Stenosis. R. B. Blacket, A. J. Palmer and E. J. Halliday.—p. 517.
 Cooley's Anaemia: Review and Presentation of Affected Family. S. J. Baker and J. J. M. O'Neill.—p. 527.
 Aids to Easy Breathing. D. G. Renton.—p. 531.
 Diphyllbothrium Latum (Linné) in Australia. D. F. Sanders.—p. 533.

2:549-580 (Oct. 27) 1951

- Role of Adrenal Cortex in Disease. K. Harrison.—p. 549.
 Emotional Factors in Allergy. D. Ross.—p. 553.
 Emotional Factors in Allergy. H. J. Prior.—p. 556.
 Osmotic Theory of Eclampsia and Mechanism of Water Retention. J. C. Edwards.—p. 559.
 The "Kink" in the Aorta. J. B. Cleland.—p. 564.

Congenital Pulmonary Valvular Stenosis.—Congenital stenosis of the pulmonary valve without overriding of the aorta or ventricular septal defect was recognized in 1859. After citing figures on the incidence of this defect, the authors stress the importance of the foramen ovale or other defect of the interauricular septum in the clinical picture. They present clinical and physiological observations on 11 cases of congenital pulmonary valvular stenosis. This lesion must always be considered in the differential diagnosis of patients with congenital heart disease, particularly in those who are not cyanotic and have basal murmurs. In severe and moderately severe cases the clinical picture is characteristic enough to be recognized by clinical methods. Mild cases in which the electrocardiogram is normal cannot be diagnosed with certainty. In both the mild and more severe cases a complicating left-to-right shunt through a patent ductus arteriosus or a ventricular septal defect may be unsuspected clinically and can be demonstrated only by cardiac catheterization. In moderately severe cases the following signs are found: (1) A systolic murmur and thrill maximal in the second left intercostal space and propagated towards the clavicle; (2) right ventricular enlargement as shown by a palpable systolic impulse between the apex and the sternum, forward projection of the right ventricle in the left oblique position at fluoroscopy, and an electrocardiographic pattern showing right ventricular hypertrophy or incomplete right bundle branch block in the precordial leads; (3) dilatation of the pulmonary artery, which may include the left main branch, with otherwise normal or diminished nonpulsatile right and left branches, and normal peripheral fields. In severe cases, in addition to the findings mentioned under (1) and (2) above, there may be a prominent "a" wave in the venous pulse, occasionally with a pulsating liver, slight cyanosis, and dilatation of the right auricle and an enlarged pulmonary artery, with small nonpulsatile branches and abnormally translucent lung fields. Severely affected patients with a small patency of the foramen ovale should be distinguished from those with a larger defect in the auricular septum. The latter are usually more deeply cyanosed and behave more as patients with the tetralogy of Fallot than as patients with "pure" pulmonary stenosis. Surgical dilatation of the stenosed pulmonary valve is practicable, but so many patients survive past middle age that the authors recommend valvulotomy only for those with a bad prognosis.

Schweizerische medizinische Wochenschrift, Basel

81:1117-1140 (Nov. 17) 1951. Partial Index

- Bronchial Asthma and Allergic Manifestations of Skin Caused by Complex Salts of Platinum; New Occupational Disease. A. Jordi.—p. 1117.
 *Immunization of Children to Diphtheria, Tetanus and Smallpox. J. R. Dreifus.—p. 1124.
 *Osteomyelitis After Trauma in Infants. R. Garsche.—p. 1131.

Immunization Against Smallpox, Diphtheria, and Tetanus.

The occurrence of postvaccinal encephalitis is reported in a male infant who was immunized against smallpox at the age of 17 months. A case is also reported of pseudovaccinal fever after immunization against smallpox in a girl aged 3 years who had pyelocystitis associated with fever. The author advocates immunization of children against smallpox between the 10th and 12th months of life provided there are no contraindications. The vaccination incision should not be longer than 1 cm., and the dose should be individualized. Vaccination should be repeated rather than too high a dose used at one time. A case of relative

failure of prophylactic immunization to diphtheria after the administration of only two doses of diphtheria toxoid is briefly reported. Two cases of serum disease after tetanus serum prophylaxis are mentioned. Immunization to diphtheria with toxoid should be carried out in children by two years of age, because resistance to diphtheria is lowest at this age, and combined diphtheria-tetanus toxoid should be employed. This method of vaccination has the advantage that immunity against both diphtheria and tetanus will be increased, and the majority of the children will be immunized to both tetanus and diphtheria. Even in children between the ages of seven and eight years, the first immunization dose should not be higher than 0.7 to 0.8 cc. The full second and third doses should be given if there was no reaction to the preceding dose. In about 400 children between the ages of 7 and 9 years who were immunized with diphtheria-tetanus toxoid (about 1,200 injections), the reactions were mild, except for occasional slight temperature elevation and local redness. In the presence of possible diphtheria infection or of a suspicious wound, a stimulating toxoid dose should be administered even one to two years after the immunization; within 4 to 10 days this stimulating dose will provide a sufficient increase of immunity. Children given serum prophylaxis should later be actively immunized to diphtheria and tetanus to exclude the risk of anaphylaxis. Since immunity can be demonstrated only after the second dose of toxoid, and since the immunity first becomes maximum five to seven weeks after the third dose, tetanus and diphtheria serum should be administered in the presence of a possible infection if five weeks have not passed since administration of the third dose of toxoid. If more than three weeks have passed since the administration of the first or second dose of toxoid, the next dose of toxoid should be given in addition to serum prophylaxis in the presence of possible infection.

Osteomyelitis Following Puncture Trauma.—The occurrence of osteomyelitis after puncture trauma is reported in two infants. The toxic condition of the first patient with coli meningitis associated with severe vomiting required the intraosseal infusion of a mixture of Ringer's solution and dextrose into the medullary cavity of the tibia. With this technique there is a greater risk of osteomyelitis than with aspiration of the bone marrow cavity for diagnostic purposes. Apparently a site of decreased resistance may be created by prolonged infusion. Frequently infection seems to be of endogenous origin rather than caused by infectious agents that have entered the puncture tract. Infants with bacteremia may often be exposed to this risk, particularly since intraosseal infusion is indicated only in severely ill infants, and then only after intravenous administration is no longer possible. Within 10 to 14 days after the infusion a roentgenologic examination should be made of the bone in which the infusion has been given, since the osteomyelitis may be clinically latent for a prolonged period. Withdrawal of blood by puncture of the heel was done for hematological examination in a second infant with erythroblastosis fetalis. An encapsulated soft tissue abscess developed from infection of the puncture canal and the inflammation extended to the adjacent bone. The osteomyelitic infection of the calcaneus caused much bone destruction. Healing of the inflammatory process in both cases followed antibiotic therapy. The fact that the sequestrum is absorbed emphasizes the value of early and prolonged treatment with penicillin and streptomycin.

Strahlentherapie, Munich

85:509-638 (No. 4) 1951. Partial Index

- Irradiation Damage to Genetic Material. H. J. Muller.—p. 509.
 Radiocobalt as Plastic Material for Irradiation Treatment. J. Becker and K. E. Scheer.—p. 581.
 Irradiation Damage to Retinal Glioma. A. Seuss and E. Stutz.—p. 589.
 *Serious Irradiation Injury After Roentgen and Radium Treatment of an Extensive Hemangioma: Carcinoma After 26 Years. L. Diethelm.—p. 594.

Carcinoma 26 Years After Irradiation of a Hemangioma.—Diethelm reports on a woman who 26 years before, at the age of 21, had had a large cavernous angioma on the right thigh, knee, and leg, which in some places had been from 2 to 3 cm. in depth. The size of the lesion made surgical treatment seem inadvisable and so irradiation was employed. The patient first had been given four roentgen irradiations at intervals of four

weeks. After this treatment had failed to produce the desired effect, radium containers were applied for 24 hours and once for 36 hours. As the result of this treatment the cavernous tissue was transformed into scar tissue, but a gradually enlarging ulcer developed that could not be permanently cured. Finally, 26 years after the irradiation, a squamous cell carcinoma developed, which necessitated amputation. The author also reports a case in which death resulted from the surgical treatment of an extensive cavernous hemangioma.

Tidsskrift for Den Norske Laegeforening, Oslo

71:665-700 (Nov. 1) 1951. Partial Index

Late Results in Hospital Treatment of Obesity. S. C. Sommerfelt.—p. 671.
Eczema Pruriginosum (Atopic Dermatitis) in Children Treated with Corticotropin. S. Hestetun and L. Wennevold.—p. 673.
Cancer in Colon and Rectum. C. Bruusgaard.—p. 675.

Pruriginous Eczema in Children Treated with Corticotropin.—Hestetun and Wennevold describe three cases of pruriginous eczema in infants treated with corticotropin (ACTH) with excellent effect. The skin affection disappeared after brief treatment, the general condition improved noticeably, the lymph node swelling in the neck receded, and troublesome itching ceased. No unfavorable effects were seen. The disorder recurred on termination of corticotropin treatment, but the eczematous skin changes in two of the patients were definitely less marked than before treatment and the general condition was better. The authors consider corticotropin indicated in treatment of infantile pruriginous eczema when the eczema is generalized and resistant to local treatment, with secondary infection and dys trophy. Treatment probably should be given for six to eight days. The patients should be hospitalized. Continuous treatment is not advised at present.

Cancer in Colon and Rectum.—Bruusgaard says that cancer of the colon and rectum should be treated by surgical means, and radiotherapy has only a palliative effect. Preoperative care is important, and is carried out to normalize the blood content of hemoglobin, protein, electrolytes, and vitamins. The intestine is given preliminary treatment with lavage, sulfonamides, and antibiotics. During the preoperative treatment the patient is given a complete general and local examination. The operative intervention consists of radical resection of the affected part of the intestine with adjoining mesentery. In the case of tumors of the cecum, ascending colon, and hepatic flexure, hemicolectomy and ileotransversostomy should be performed, in one stage. With tumors in the transverse colon, splenic flexure, descending colon, and the proximal two-thirds of the sigmoid, colon resection is done with end-to-end anastomosis in one or two stages. With tumors in the rectum and rectosigmoid, abdominoperineal resection is performed with permanent colostomy in the proximal sigmoid loop. In patients admitted with acute ileus, abscess formation, or poor general condition, the introductory operation is the creation of a simple intestinal fistula proximal to the stenosed part. The importance of adequate after-care is stressed. The operative mortality in radical operations is at present between 3 and 6%. The percentage of cures after five years is estimated to be between 45 and 60%.

Ugeskrift for Laeger, Copenhagen

113:1473-1502 (Nov. 1) 1951

*Recurrent Palmoplantar Pustulosis (Dore's Acrodermatitis). B. Heilesen and R. Hornbech-Madsen.—p. 1473.
Cases of Cancer of Pancreas Diagnosed Roentgenologically by Lateral View of Stomach. E. Hovesen.—p. 1479.

Recurrent Palmoplantar Pustulosis.—An average of 3% of the new patients treated in the Finsen Institute's skin clinic have palmoplantar pustulosis (Dore's acrodermatitis). From 1945 to 1950 treatment was given in 142 cases, of which 43% were in men and 57% in women. The disorder begins after puberty; 60% of the patients were between 20 and 39, 32% were between 40 and 59, only 4% were under 20, and 4% were over 60. Both hands and feet were affected in 65% of the cases, hands only in 18%, and feet only in 10%; in 7% the disorder was unilateral. In 17% of the cases psoriasis was present in other parts of the body and a pathogenetic relation between the two disorders is

suggested. Treatment with penicillin (300,000 units daily for 10 days) resulted in disappearance of the pustulosis or improvement in 80% of the patients, and 38% remained free from symptoms for at least a year. Comparison with cases treated with Dreuw's ointment (an ointment of salicylic acid and chrysarobin with birch tar oil) and radium irradiation showed that of these cases only 14% were free from symptoms after a year. Clinically no difference was seen between the cases that seemed to be related to psoriasis and those that apparently depended on bacterial activity.

Wiener medizinische Wochenschrift, Vienna

101:889-908 (Nov. 24) 1951. Partial Index

*Therapy and Prophylaxis of Tuberculosis in Childhood. H. Frey.—p. 890.
Hearing Difficulty Due to Noise and Its Prevention. E. H. Majer.—p. 892.
Experiences with Aureomycin in Pertussis. E. Martschnig and W. Rittner.—p. 895.

Therapy and Prophylaxis of Tuberculosis in Childhood.—With Calmette's BCG vaccine about 80% of healthy children can be immunized against tuberculosis. Children with a positive reaction to Mantoux' or Pirquet's tests may no longer be considered healthy and consequently should not be vaccinated with BCG vaccine. Because of the large number of these children who have become infected with tubercle bacilli and who are in the initial stage of the disease, it seems most urgent that clinical progression of tuberculosis may be prevented by early and adequate treatment. Several hundred children who had been exposed to tuberculosis or already had become infected were treated by the author with a suspension of extensively modified (no longer acid-fast) and killed tubercle bacilli (VMT liniment). It was applied percutaneously to the skin of the antecubital fossa. The original vaccine contained 1,000 million bacilli per cubic centimeter from which a liniment was prepared by dilution in four concentrations of 125 million, 250 million, 500 million, and 1,000 million bacilli per cubic centimeter, respectively. Inunctions were made by the child himself with his index-finger using gradually increasing doses of one to four drops of the liniment at three day intervals alternately on the right and left forearms, starting with the 125 million bacilli concentration and using one of the four concentrations after the other, until the highest dose of four drops of the highest concentration of the liniment had been applied 8 to 10 times according to the individual case and its course. In about 90% of the patients there was a pronounced favorable change in the general condition within a few weeks. The appetite was increased, with resulting increase in weight. Elevated and subnormal temperatures were restored to normal in 80% of the patients. Dry cough subsided, and in patients with expectoration the sputum contained less pus and decreased in amount. The children tended to have fewer colds and the size of the lymph nodes diminished. Refractory scrofulous inflammations of the children's eyes healed completely within several weeks, and there were no more recurrences. The use of the VMT vaccine made from modified and killed tubercle bacilli for large scale clinical trials seems desirable to determine whether it may increase the defense power of the organism.

Zeitschrift für klinische Medizin, Heidelberg

148:431-532 (No. 5) 1951. Partial Index

TB I in Treatment of Tuberculosis in Patients with Diabetes. K. Repke.—p. 431.
Changes in Ganglion Cells Caused by Hypoglycemia. W. Hopker.—p. 448.
Rotation Factor in Left-Sided Hypertrophy and Its Electrocardiographic Manifestations. H. Gillmann.—p. 473.
*Suicide with Insulin. M. Güllow.—p. 479.

Suicide with Insulin.—Güllow describes a man, aged 39, who had diabetes; because of poor metabolic adjustment of his diabetes and relapsing hepatitis he was subject to hypoglycemic reactions. Without having eaten anything for 12 hours, he gave himself (with suicidal intention) an injection of 400 units of insulin. Circumstances made it impossible to begin treatment of the severe hypoglycemia before five and a half hours had elapsed. Treatment was ineffective. Necropsy revealed, in addition to the chronic hepatitis, an extensive intrameningeal hemorrhage and signs of cerebral pressure, which are regarded as the cause of death.

BOOK REVIEWS

How to Keep Our Liberty: A Program for Political Action. By Raymond Moley. Cloth. \$4. Pp. 339. Alfred A. Knopf, Inc., 501 Madison Ave., New York 22, 1952.

Every American eligible to vote in 1952 should read this book. It is the most complete exposition of the dangers confronting this constitutional republic from statist attack that has been published. In dignified and restrained language, Mr. Moley traces the growing peril to our liberty of the political and ideological trends of the last 20 years. The basic theses of the founders of the republic are briefly reviewed, followed by a detailed analysis of the manner in which their noble aims have been perverted and distorted by movements that have almost but not irrevocably destroyed the fundamental internal structure of the republic.

Mr. Moley has scrupulously avoided the dramatic, overzealous approach. He has presented carefully reasoned and incontrovertible evidence of socialist thinking and motivation in the present administration's activities in medicine, industry, agriculture, banking, education, and other areas.

Positive answers are proposed to the innumerable problems that confront the nation, and the ways in which those problems can be met within the framework of our traditional liberties are outlined in detail. Finally, Mr. Moley presents a plan for organized political action by citizen groups, with special emphasis on the mobilization of the great middle-income group, whose freedoms are particularly under attack but whose political actions are relatively unorganized and ineffectual.

This is in a sense a conservative manifesto, and its influence will be felt for many years to come. Socialists who read this book should think twice before continuing to promote their theories, and those interested in the preservation of this country will be provided with an enormous amount of documentary material with which to substantiate their arguments.

Here is a call for militant political action to halt the progressive impairment of our free institutions, to improve the capacity and integrity of our federal government, and to build a sound, prosperous future while retaining the genius of our checks and balances system.

Tobacco and the Cardiovascular System: The Effects of Smoking and of Nicotine on Normal Persons. By Grace M. Roth, Ph.D., Associate Professor of Experimental Medicine, Mayo Foundation for Medical Education and Research Graduate School, University of Minnesota, Minneapolis. Publication number 100, American Lecture Series, monograph in American Lectures in Circulation. Edited by Irvine H. Page, M.D., and A. C. Corcoran, M.D. Cloth. \$2.25. Pp. 66, with 8 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford; Ryerson Press, 299 Queen St., W., Toronto 2B, 1951.

Because of the controversy concerning the effects of smoking and nicotine on the cardiovascular system, Dr. Roth performed carefully controlled experiments, using normal persons. The subjects were habitual smokers who inhaled while smoking. Careful physiological and metabolic observations were made with different brands of cigarettes, different types of cigarette paper, filters and no filters, unlighted cigarettes, and even corn silk. No changes were noted when a cigarette was puffed but not lighted and when corn silk was smoked. In all other cases in which tobacco was used and in which the cigarette was lighted, there was a decrease in the cutaneous temperature of the extremities, indicating vasoconstriction. To determine whether this effect was due to nicotine, it was administered intravenously, and similar effects were obtained; however, these effects did not occur if saline solution was given. After smoking two cigarettes, the average blood pressure increases were 19 mm. Hg systolic and 14 mm. Hg diastolic, and the pulse rate increased an average of 36 beats per minute. The electrocardiographic changes caused by smoking consisted of an increase in the heart rate,

lowering of the amplitude of the T wave, and, in one person, the T wave became inverted. Investigation determined that habitual smokers showed no evidence of acquiring tolerance to the effects of smoking, and it was demonstrated that the effects of smoking were due to the nicotine.

The changes in the cardiovascular system were less marked if the nicotine content was low, but the nicotine content of the cigarette had to be decreased at least 60% in order to decrease the vascular effects. There was, however, a great variation in the amount of nicotine in the so-called denicotinized cigarettes. The amount of nicotine in these cigarettes is not sufficiently decreased to protect one against the effects of smoking. In order to determine whether alcohol would prevent vasoconstrictive effects of tobacco, patients were examined after smoking cigarettes following ingestion of alcohol. It was demonstrated that vasoconstriction from smoking could not be prevented by alcoholic vasodilatation. This monograph is a valuable contribution and should be in the library of every physician treating patients with cardiovascular disorders or those in whom there is a family history of such disturbances.

The Enzymes: Chemistry and Mechanism of Action. Volume II, Part 1. Edited by James B. Sumner and Karl Myrback. Cloth. \$14.80. Pp. 790, with illustrations. Academic Press, Inc., 125 E. 23rd St., New York 10, 1951.

This book is the third in a series that surveys the field of enzyme chemistry. It aids in evaluating the progress made in this field, and, at the same time, it helps to focus attention on areas requiring more clarifying work. The volume consists of 21 chapters; the majority deal with the enzymes involved in phosphorylation, decarboxylation, dehydrogenation, and oxidation. Among the subjects included under phosphorylation are thermodynamics and the mechanism of the phosphate bond, transphosphorylation, dephosphorylation, and the enzymes, aldolase and isomerase. The decarboxylation chapters includes discussion of the keto and amino acid decarboxylases and a brief description of desulfinate, an enzyme comparable to the decarboxylases, which causes the decomposition of sulfinic acids. Among the dehydrogenases are codehydrogenase 1 and 2, the apoenzymes, and succinic dehydrogenase. A chapter is devoted to the enzymes that cause hydrogen to be evolved, namely, hydrogenase and hydrogenylase. Enzymes involved in oxidation are discussed under the flavin-containing enzymes, the iron-containing enzymes, the copper-containing enzymes, and the oxidases, which are specific for amines, amino acids, and unsaturated fats. Two associated chapters discuss the oxidation of organic sulfur compounds and the phenomenon of luminescence. Single chapters are devoted to the theory of oxidation-reduction, anaerobic glycolysis, respiration and the Pasteur effect, and yeast and mold fermentation.

The book cites many appropriate references, including much recent material. The volume has no index, but the next number of the series will include the index for parts one and two of volume 2.

Your Mind and Appearance: A Psychological Approach to Plastic Surgery. By Adolph Abraham Apton, M.D. Cloth. \$3. Pp. 212, with 28 illustrations. Citadel Press, 120 E. 25th St., New York 10, 1951.

Psychological reactions to various physical defects is the main theme of this work. The author attempts to describe emotional traits and adjustments and maladjustments occurring in life in relation to all periods of development. The subject matter, therefore, is divided according to the infancy and childhood, adolescent, adulthood, and aging periods. The author reminds the practitioner that deformities or malformations may have profound and lasting effects on the economic and social status of a person, as well as on his personality. He stresses the fact that early surgery can prevent subsequent psychic trauma.

The jumble of quotations interspersed in the text, plus numerous repetitions, make it difficult for the reader to follow a coherent thought or to extract the author's own views on a given

subject. The many testimonials and the overwhelming number of case reports tax the reader's patience. Twenty-eight plates constitute a group of illustrations showing facial features before and after surgical intervention. In his preface, the author states illustrations were limited owing to the fact that patients object to publication of their photographs. There are, however, numerous ways of circumventing such objections. Illustrations are not convincing unless the actual unretouched photographs are reproduced. The book is intended for both layman and physician; the former would probably benefit more than the latter.

The Facts of Life from Birth to Death. By Louis I. Dublin, Ph.D., Second Vice-President and Statistician, Metropolitan Life Insurance Company, New York, in collaboration with Mortimer Spiegelman, F.S.A., Assistant Statistician, Metropolitan Life Insurance Company. Cloth. \$4.95. Pp. 461, with 22 charts. The Macmillan Company, 60 Fifth Ave., New York 11, 1951.

Dublin, during his 40 years as the statistician of the Metropolitan Life Insurance Company, has had an opportunity to study a wealth of factual data dealing with various aspects of life. In addition to using the data generally available to all statisticians, he has developed and used many valuable statistics from the records of the industrial policyholders of his company. This book is a summary of this wide range of data, and it highlights those statistics that are of interest to the general public. He has included chapters on the increase, distribution, and changes in the age and racial composition of the American population; factors influencing the rates of reproduction and marriage; data on the composition and financial status of the average American family; and marital dissolution by divorce, separation, and death. Separate chapters are devoted to statistics on tuberculosis, cancer, diabetes, pneumonia and influenza, circulatory diseases, and rheumatic diseases; he compares the past and present prevalence, cures and control, and mortality rates of these diseases. The hazards peculiar to infancy and childhood and the many problems arising because of the increase in the number of old persons in our society are discussed. The various elements of the accident toll, the hazards of some occupations, and human impairments are also discussed. Other chapters deal with homicide and suicide, mental health, longevity, body structure, public health agencies and their operations, and the effects of war on the entire population.

The emphasis upon public health rather than the practice of medicine will not detract from the usefulness of the volume for physicians. The reader should be warned, however, on one small point; not until page 405 does one get the distinction between average length of life and expectation of life at birth. Physicians and other readers frequently confuse these two terms. The distinction becomes clear in the following quotation: "For example, men born in 1890 will have an average length of life of about 4.2 years longer than the expectation of life at the time of their birth." It is unfortunate that the author did not distinguish between these two terms when they were first discussed on pages 386, 387, and 395. One might also wonder why life expectancy at birth in the United States (49.2 years) for 1900 to 1902 is used in tables and charts for long term comparisons in the chapter entitled "How Long We Live" now that Greville has given us a figure of 47.3 years for life expectancy at birth in 1900.

The book is written in question and answer form to facilitate easy reference to specific inquiries. Each chapter has been supplemented with selected references for the benefit of those who desire information beyond the main points covered in the text. This volume is an extremely useful reference work for all persons interested in vital statistics.

Frontiers in Medicine: The March of Medicine, 1950. New York Academy of Medicine Lectures to the Laity, no. 15. Cloth. \$2.50. Pp. 150, Columbia University Press, 2960 Broadway, New York 27, 1951.

This volume consists of six articles dealing with recent developments in various phases of medicine, including sociologic psychiatry, control of acute and chronic diseases, medical genetics, a mechanical heart-lung apparatus, antibiotics, and concepts and methods of medical research. The authors, renowned authorities in their field, present material that is both interesting

and provocative, and which is worthy of reading by physicians and all those interested in medical progress. The reader may review many important recent strides forward in medicine and catch a glimpse of the possibilities that lie ahead. This book deserves a place on the shelf with the others of this series.

Diseases of the Ear, Nose, and Throat: A Textbook of Clinical and Laboratory Procedures. By Georges Portmann, M.D., Professor of Otorhino-laryngology at University of Bordeaux, Bordeaux. Translated by Fernand Montreuil, M.D., and Jules G. Waltner, M.D. Cloth. \$20. Pp. 728, with 677 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1951.

The author of this book is familiar to a generation of American otolaryngologists who participated in European postgraduate work in the interval between the two world wars. The book itself is a summary of his teaching at Bordeaux and Paris and is directed to the full-fledged specialist as well as to the resident physician in training. The author commences with an anatomic, physiological and pathological discussion of the various organs concerned in this specialty. He then describes his method of taking a history and follows this with a comprehensive description of his methods of clinical examination. He maintains that adherence to basic rules will reduce diagnostic errors to a minimum.

The book contains considerable material not evident in orthodox American textbooks on otolaryngological practice. American specialists will find much data useful but will find other information inapplicable to the American medical scene; for example, the author asserts that catheterization of the maxillary sinus is being replaced increasingly by antra puncture; actually, the reverse is true in the United States. Nevertheless, this book contains excellent source material for American otolaryngologists. Its usefulness as an introductory textbook for the novice who has not completed his residency is doubtful. This work can be read with profit by those who teach undergraduate and postgraduate students; many of the author's ideas can be modified and utilized for teaching purposes.

A Textbook of Pharmacology and Therapeutics. By Harold N. Wright, M.S., Ph.D., Professor of Pharmacology, University of Minnesota, Minneapolis, and Mildred Montag, Ed.D., R.N., Assistant Professor of Nursing Education, Teachers College, Columbia University, New York. Fifth edition. Cloth. \$4.50. Pp. 620, with 77 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1951.

This textbook has been written primarily for students of nursing. The more important advances in the field of pharmacology are adequately covered. The authors devote chapters to different types of preparations and the coloring and flavoring of medicines. Drugs are classified according to their actions on physiological systems. The authors are to be commended for their review of the physiology of each system before introducing the reader to its pharmacology. A well-presented chapter on oxygen therapy and therapy with other gases, and one on toxicology are included. The bioassay of drugs and an explanation of U. S. P. units and other biological standardization units have been omitted.

Psychology in the Service of the School. By M. F. Cleugh. Cloth. \$3.75. Pp. 183. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1951.

The points made in this book, by an English author, have as much significance as do discussions by American authorities. An unusual feature is the fact that ordinary, everyday problems are considered. Because it is often from these minor deviations that serious maladjustments develop, teachers and others in charge of children should appreciate and understand the best methods of applying corrective measures at the start. In an extensive introduction, the author writes a scholarly and readable review of the present status of psychology in education. In addition to chapters on the meaning of maladjustment, the handling of aggressive and regressive reactions, and a special discussion of numerous examples, there is a chapter on a practical guide for action, in which desirable procedures are itemized and discussed. Physicians with school affiliations will find this book of interest and assistance.

EXPOSURE TO SILVER DUST

TO THE EDITOR:—*A few times a year, for periods of two or three days, some of our employees are exposed to the dust of metallic silver; they are covered with it from head to foot. Even though provided with coveralls, rubber gloves, and fresh air masks under positive pressure with plastic hoods, a certain amount of the dust is absorbed. On occasion, these workers are also exposed to solutions of silver nitrate, which temporarily stain their skin. I should like to know what techniques are available for determining the silver concentration in the blood or urine? Is there any test to estimate or predict the amount of silver that can be absorbed before permanent discoloration of the skin occurs? Are there any systemic effects that could be attributed to the absorption of metallic silver?*

M.D., West Virginia.

ANSWER.—The soluble salts of silver, such as silver nitrate, are toxic, and fatalities have occurred. These may not be attributable to silver, per se. No standards of concentration of exposure have been established above which argyria becomes prospective. Variations in susceptibility are pronounced. In some European industries employing silver, such as bead manufacture, localized surface deposits of silver are nearly universal. The scleras are often first involved. Apart from cosmetic damage, skin deposits are believed to be without importance. Only small amounts of silver are excreted through the urine, it is excreted instead through the intestinal tract. Precise urinary determinations require spectrographic procedures. (Kehoe, R. A.; Cholak, J., and Story, R. V.: Manganese, Lead, Tin, Aluminum, Copper, and Silver in Normal Biologic Material, *J. Nutrition* 20: 85, 1940.) A crude chemical method, chiefly qualitative, but roughly quantitative, may be carried out in the following manner. A small cylinder of zinc, wrapped with a thread of platinum, is submerged in the urine. Silver, if present, deposits on the platinum. This becomes visible after exposure to nitric acid fumes. But, as the thread of platinum is rubbed on white paper moistened with ammonium hydroxide, a deposit of silver will appear. This becomes black if the paper is then moistened with a solution of hydrogen. This has no great diagnostic value. Apart from the well-established toxic properties of soluble silver salts and apart from possible dermatitis, the silver ion is regarded as harmless (except for argyria).

A few cases have been described in the literature mentioning gastrointestinal pathology (Heiman, H.: Toxicity of Metallic Silver, *Indust. Hyg. Bull.* 22:81, 1943). Other metals constituting impurities of silver, such as lead, may account for all instances of alleged silver poisoning.

RATTLESNAKES

TO THE EDITOR:—*A patient has just moved into a mountainous area near Los Angeles. There are many rattlesnakes, two having been killed on the acreage in the first week. The patient wishes to know: 1. Is there some poison or other way of driving them away? 2. If one of her children were bitten, what equipment should be kept on hand for such an emergency and what should be done?*

Richard Thomas Barton, M.D., Beverly Hills, Calif.

This inquiry was referred to two authorities, whose respective replies follow.—Ed.

ANSWER.—There is no good way to drive rattlesnakes away. Their numbers can be kept down by removal of objects that serve as cover for them, such as rotting wood, flat stones, and brush piles. Local doctors should keep on hand equipment necessary for the treatment of snakebites. Then, if a person is bitten, a loose tourniquet should be applied just above the bite and the victim rushed to the doctor. A "loose" tourniquet is one that does not shut off the flow of blood in the deep blood vessels, i. e., does not stop the pulse but does shut off the flow of blood and lymph in the superficial vessels. It is best to teach children a good deal about the local snakes, so that they will not be needlessly terrified of the numerous harmless species but will at once recognize a rattlesnake. They should know that, in California, only the rattlesnake is venomous. Good nontechnical accounts of the snakes of southern California can be secured from the Zoological Society of San Diego, San Diego 12, Calif.

ANSWER.—1. The best way to discourage rattlesnakes around one's home is to eliminate wood piles and areas that harbor rats and mice, as they are attracted by these rodents. 2. Secure a first aid kit from any manufacturer that makes the suction kit. It is wise to open the kit, read the directions, and practice using suction on the hand or foot.

INHERITANCE OF CYSTIC DISEASE OF THE PANCREAS

TO THE EDITOR:—*A woman whose first child died of cystic disease of the pancreas has since had another child who is apparently normal. She fears having another pregnancy because she has been told that any further children are likely to have the same disease. Is there any evidence to support this fear?*

Joseph I. Echikson, M.D., Newark, N. J.

ANSWER.—The literature on this subject clearly shows that the expression of fibrosis of the pancreas depends on the recessive type of heredity. In order to have the disease, a child must have the two appropriate recessive genes, one of which comes from each of the parents, who do not have the disease but who carry one gene each for it. In the present instance the loss of a child with cystic disease of the pancreas shows that both parents carry the gene. Consequently, there is one chance in four at each subsequent pregnancy that the child will have the disease. The parents themselves must decide whether they wish to risk losing another child. As yet, there seems to be no permanent cure for this disease.

EXPOSING A FOREIGN BODY NEAR THE LESSER TROCHANTER

TO THE EDITOR:—*Please indicate the best route to approach a foreign body located at the lesser trochanter, and what muscular layers would be traversed in exposure.* *M.D., New York.*

ANSWER.—The easiest approach to a foreign body in the region of the lesser trochanter of the femur is an anterior approach, with a skin incision beginning just below the anterior-superior iliac spine and directed downward for a distance of 4 to 6 in. (10.16 to 15.24 cm.). The incision should be carried down between the tensor fasciae femoris and sartorius muscles. The rectus femoris could be reflected laterally, and this would give direct exposure to the lesser trochanter. It would probably be necessary to ligate and sever the lateral femoral circumflex vessels, which traverse this plane. The femoral nerve should be reflected laterally along with the rectus muscles. This exposure will bring into view the iliopsoas muscle, and this can be followed to its insertion on the lesser trochanter of the femur.

FREIBERG'S DISEASE

TO THE EDITOR:—*I have a patient who has had Freiberg's disease for five years; the symptoms are broadening of the head of the second metatarsal and outer articular calcium deposits. Kindly advise as to treatment.*

A. A. Skemp, M.D., La Crosse, Wis.

ANSWER.—In most cases, conservative treatment has made operative procedure unnecessary. However, in advanced cases, with marked alteration of the head of the metatarsal bone and loose bodies in the joint, correction by operation has been suggested. The loose bodies are removed through a small dorsal incision, and the rough irregular head is made smooth by means of a small, curved chisel. Removal of the head of the metatarsal bone is not advised, since this increases the strain on the heads of the others.

PENICILLIN AND EPINEPHRINE

TO THE EDITOR:—*Would it be permissible to give aqueous penicillin and epinephrine, 1:1,000, mixed in the same hypodermic syringe?*

Edward S. King, M.D., Shelby, N. C.

ANSWER.—There are no objections to giving aqueous penicillin and epinephrine, 1:1,000, mixed in the same hypodermic syringe when both agents are indicated in treatment.

UNNATURAL PHENOMENA

TO THE EDITOR:—*Can the weird ghost scenes and sudden religious conversions said to be experienced by some susceptible persons be ascribed to back flashes of the optic nerve upon the retina? Please explain this psychosomatic phenomenon.*

Walter A. Landry, M.D., Chester, Pa.

TO THE EDITOR:—*Is there any physiopathological change in the eye or the brain accompanying the following complaint? An 18-year-old male complains of seeing words before his eyes, as others complain of seeing "spots" before their eyes. The words are not usually associated with his thinking processes at the time. The images may occur any time during the day, although probably more frequently when he is tired. This condition has been present for two to three years. The words appear only in black. Lesions of the lenses, media, or fundi were not found. The patient has 1 diopter of hyperopia. He is a diabetic, controlled at present with 40 units NPH insulin daily.*

M.D., Ohio.

ANSWER.—Visual sensations are produced by the images, formed on the retina, of objects in the outside world. However, this is only the first step in seeing. After the impulses in the optic pathways reach the brain, they are integrated and synthesized with other sensations, and especially with visual memories, to produce visual perceptions. It is well known that light falling on the retina, technically called the adequate stimulus, is not the sole means by which the rods and cones can be stimulated. Mechanical pressure applied by the finger tip on the posterior part of the eye suffices to stimulate mechanically the rods and cones; they can also be stimulated by an electric current. The cerebral centers can be stimulated by a blow on the head, which makes one see "stars." The cerebral cortical cells, which store up memories, can bring images into consciousness. Think of the infinite store of visual memories so close to the surface of consciousness that they are available for instant comparison with and elucidation of present sensations! It is not surprising that there are sundry other ways in which memory pictures can reach the surface of consciousness. Obviously, the emotions will exert a marked influence, as will the many and varied features of dreams. Thus, the elements are present to account for the phenomenon of "seeing things," whether words, faces, scenes, or events. Although we are a long way from complete knowledge of the physical and chemical processes that take place, we are neither justified in introducing a hypothetical supernatural explanation nor justified in calling these sensations imaginary. The phenomena are very real and subject to the laws of cause and effect. Their seat is not peripheral but is in the higher centers. They are normally controlled by inhibition and suppression. They are psychological in nature and must be studied by a psychological approach.

Picture the infinite store of past experiences capable of being tapped and brought to consciousness, usually under control but not infrequently seeming to break away from the natural laws. It is only our restricted knowledge that creates a class of what we may be tempted to call unnatural phenomena.

PREMATURE GRAY HAIR

TO THE EDITOR:—*A boy, aged 7, for a year and a half has had a marked increase in gray and white hair in his scalp. He has both food and pollen allergies and as an infant had moderate eczema. He is being treated for allergies, on a Rowe elimination diet, and receives seasonal desensitization for his pollen allergies. This therapy controls his hay fever and asthma. I would appreciate any information as to further treatment and diagnostic studies.*

Mervin J. Chaffin, M.D., Waterford, Calif.

This inquiry was referred to two consultants, whose respective replies follow.—ED.

ANSWER.—This boy may have leukotrichia, which is similar to vitiligo or leukoderma of the skin. Treatment is unsuccessful. There has been some suggestion in recent years that psychogenic factors might have etiologic significance. There has been an unsubstantiated report that the administration of paraaminobenzoic acid is sometimes of benefit, although there have been numerous reports of failure from such treatment.

ANSWER.—The graying of hair in pantothenic acid-deficient dogs, and less so in riboflavin, folic acid, and biotin-deficient dogs, as shown by Dr. Agnes Fay Morgan of the University of California, suggests that such deficiencies may cause graying in man. Proof of this, however, has never been presented. The Rowe elimination diets, as published, include ample amounts of these vitamins and call for supplemental B as well as other vitamins. Thus the diet, if prepared according to directions, would not be a likely cause. Those physicians, moreover, who have used these and other adequate trial diets for the study and control of food allergy for years have not encountered such graying of hair. Since this therapy effectively controls the hay fever and asthma, it should be continued. It is possible that inheritance may explain this premature gray and white hair.

PLASTIC EARDRUM

TO THE EDITOR:—*Is the treatment for deafness with a plastic eardrum recognized as being an acceptable scientific method?*

M.D., Georgia.

ANSWER.—The artificial plastic eardrum has been used with some success in cases in which deafness was due to an absent or diseased middle ear, which mechanically prevented sound from reaching the cochlea. Earlier, the destroyed nonfunctioning sound conduction apparatus was replaced with a diaphragm rod prosthesis, which did not prove to be very practical, because the average ear canal was too narrow and tortuous to accept this insert. Subsequently, a less efficient, but more easily applied middle ear prosthesis was developed in the form of an artificial eardrum. In selected cases, this device has proved to be of help in improving the hearing.

PRINTING MATERIALS AND CONTACT DERMATITIS

TO THE EDITOR:—*A patient has contact dermatitis on the volar surface of the forearms. He handles hot lead in a printing shop. He is slightly sensitive to several foods; these have been eliminated. Are patch tests with lead advisable?*

Howell E. Leming, M.D., Fayetteville, Ark.

ANSWER.—Metallic type used by compositors in the printing industry is an alloy consisting of lead, antimony, and tin, any of which is capable of producing dermatitis in susceptible persons. However, dermatitis in printers is more likely to be due to inks or to the various alkalies and solvents used to clean the type and presses. The latter consist of such materials as turpentine, xylene, benzol, soda ash, and trisodium phosphate. Patch tests may be performed with the metallic substances or with the inks but not with the solvents.

FLUORIDE BY MOUTH DURING PREGNANCY

TO THE EDITOR:—*Will fluoride given to the mother by mouth during pregnancy cause the baby to have better teeth in life?*

Needham B. Bateman, M.D., Atlanta, Ga.

ANSWER.—There is no evidence that fluoride taken by the mother during pregnancy will cause a baby to have better permanent teeth. Since the tooth buds of the permanent teeth are not even formed at the time of birth, it is difficult to see how fluoride can affect the baby's future teeth in utero.

GYNECOMASTIA IN A YOUNG BOY

TO THE EDITOR:—*The answer on gynecomastia on page 909 Queries and Minor Notes, in THE JOURNAL, Oct. 27, 1951, omitted one of the most frequent causes of this condition. Mitchell and Nelson (Textbook of Pediatrics, ed. 5, Philadelphia, W. B. Saunders Company, 1950, p. 1416), reported that "gynecomastia or unusual enlargement of mammary tissue is a frequent occurrence of adolescent boys. Spontaneous regression is usually observed when maturation takes place. In the patient described, watchful waiting combined with psychotherapy would seem to be the best treatment."*

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PROPER USE OF IRON, LIVER EXTRACT, VITAMIN B₁₂, AND FOLIC ACID IN ANEMIAS

Frank J. Heck, M.D., Rochester, Minn.

In the past 25 years the methods of treating the anemias have undergone striking changes which have made necessary, attention to accurate classification and grouping of patients. It is interesting that thinking in regard to the use of iron should have changed so radically at approximately the same time that treatment with liver was introduced, yet this change was the natural outcome of the extensive research carried on by Whipple and his associates and many other workers in the field. It was probably only natural, too, that after demonstration of the amazing response of pernicious anemia to liver this material should be tried in other types of anemia.

The introduction of liver extract and desiccated hog stomach for oral use and, later, of extracts for parenteral use further accelerated the tendency of members of the medical profession to use many different preparations in the treatment of anemia without paying much attention to whether the treatment was basically sound or had a background of proved practical merit.

The production of certain liver-stomach concentrates in combination with other medicaments and the exploitation of these preparations through the detail men of certain pharmaceutical houses have led to a tremendous expenditure of money from which little if any benefit has been derived. Although some benefit may have been obtained from some of these products, the substitution of other simpler preparations would have resulted in the same benefit at a 10th or a 20th of the cost.

Consider the position of the medical profession if a nationally distributed magazine should choose to present the evidence concerning the value of some of these widely promoted combination preparations that lack the stamp of approval of the Council on Pharmacy and Chemistry of the American Medical Association, preparations that are being passed on to the public by the medical profession without adequate scientific evidence of their therapeutic value. Accurate figures as to cost of these preparations are not available, but it has been estimated that their sale value for the year 1948 was 31 million dollars.

Among hematologists generally, the use of preparations of this type is much decried, and in the past several years several editorials have expressed disapproval of treatment with such preparations. Yet the literature of today is replete with instances in which mixed treatment consisting of preparations of iron and the various preparations of liver or liver and stomach are being used. It has become a common experience to see patients who have recently been treated with preparations of liver and of stomach, alone or in combination, who by no stretch of the imagination could be considered to have been anemic. Except possibly in some unusual situations the treatment of anemia depends on the use of specific substances according to the blood picture.

USE OF IRON

Indications.—From the purely practical standpoint of treatment there should be no question as to what preparation should be used in all but a small fraction of the cases of anemia. The great bulk of all the anemias amenable to treatment fall in the group of iron deficiency or hypochromic anemias, in which the anemia has developed as a result of loss of blood or inadequate intake or inadequate absorption of dietary iron from the gastrointestinal tract. Relatively few cases belong in the last two groups, the great majority being due to loss of blood. Moore¹ has recently made "idiopathic hypochromic anemia" the subject of an editorial. He pointed out that, although it may require two or three years of observation to demonstrate the cause of the iron deficiency, if each patient is adequately observed over a long enough period, the cause can be explained, and for this reason the term "idiopathic hypochromic anemia" should be deleted from medical literature.

Preliminary Considerations.—A preliminary to consideration of the use of iron as a therapeutic agent is careful investigation of the anemic patient. Anemia is a symptom, not a disease; thus, when the physician prescribes treatment for anemia without ascertaining the cause, he is perhaps indulging in dangerous symptomatic treat-

From the Division of Medicine, Mayo Clinic.

Read before the General Scientific Meetings at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 12, 1951.

1. Moore, C. V.: "Idiopathic" Hypochromic Anemia—An Obituary, *Blood* 5: 876 (Sept.) 1950.

ment. In generations past the practice of prescribing iron for patients who complained of weakness or fatigue was so commonplace that in the mind of the laymen these two symptoms were and still are almost synonymous with anemia. A careful evaluation of nutrition and growth up to and including puberty, systematic inquiry into the amount of blood lost with menses, rapidly recurring pregnancies or miscarriages, and detailed information as to possible loss of blood by any other route must be obtained. This information, of course, is acquired in taking a good general history, and in the presence of hypochromic anemia it becomes especially important. In women the problem is frequently easily solved by the history of menorrhagia, but, in the absence of excessive flowing, the problem in the female, just as in the male, becomes one of excluding by all possible means the presence of a bleeding lesion.

It is probably well at this point to interpose a few statements regarding the metabolism of iron.

It is estimated that a well-balanced diet in northern United States contains 10 to 12 mg. of iron daily. All of this iron, however, is not available for conversion into hemoglobin. Earlier estimates gave the maximal possible absorption at about 50% of the total iron contained in the diet. It seems likely that this figure is rarely attained. Granick² recently estimated that absorption was more likely to be in the range of 0.5 to 1.5 mg. of iron per day. Furthermore, the daily rate of absorption is inconstant even when the need for iron is great. Present and past studies have shown that absorption of iron occurs in a cyclic manner. Absorption normally occurs in the first few inches of the duodenum, and experimentally this phenomenon can be demonstrated by the staining of ferritin granules in the mucosal cells. These cells can reject iron, but the exact mechanism controlling this action is not well understood. For normal persons the maximal excretion of iron, as the result of wear and tear on iron-containing cells, is probably 1.0 mg. per day. Even with oral administration of pure soluble ferrous salts, the form in which iron is absorbed from the gastrointestinal tract, only a relatively small portion of the iron so administered is absorbed. However, iron salts given intravenously are converted quantitatively into hemoglobin. In general, iron so given is retained tenaciously by the body, although a small proportion may be excreted in the urine as demonstrated recently by Scott and Govan.³ In the older literature the observation is reported that the concentration of hemoglobin of patients who have had a severe loss of blood improves at an average rate of approximately 1% in four days when the diet is good. If it is assumed that 50% of the average quantity of 12 mg. of iron in the diet is absorbed per day, then this increase of 1% in the concentration of hemoglobin would require utilization of approximately 25 mg. of iron. In spite of recent observations that the amount of iron absorbed may not be nearly as great as originally thought, it has been found, on administering iron intravenously, that dosage of iron calculated on this basis (25 mg. for each 1% deficit in hemo-

globin) gives on the average an increase of hemoglobin that closely approximates this theoretical value.

Physiologically the periods of greatest need for iron are (1) in infancy, (2) during puberty, (3) to replace iron lost through menses, and (4) during pregnancy and lactation. Aside from these periods, only sufficient iron is needed to replace that lost through wear and tear. The appearance of a hypochromic anemia in a male after the period of growth is completed or in the female after the climacteric demands an explanation on the basis of some type of loss of blood.

Morphologically the chief characteristic of iron deficiency anemia is hypochromasia. Often there is a well-defined microcytosis, but the cells may vary from microcytic to normocytic. Although achlorhydria may be found and is a common accompaniment of a certain group of anemias of women during menstrual life, in the ordinary case of iron deficiency anemia, absence of free hydrochloric acid can be expected to occur with the same frequency that it would be expected in any other group of persons.

Oral Administration.—After the cause of the iron deficiency is determined, whether from loss of blood or for a nutritional reason, the problem of treatment must be considered. This has two aspects: (1) elimination of the underlying process if feasible and (2) specific therapy to relieve the iron deficiency. The first aspect is beyond the scope of this paper. The latter consists in the administration of simple ferrous salts by the oral route. Ferrous sulfate, carbonate, or gluconate are among those most commonly used, and these are given in a dosage of 15 to 30 grains (1 to 2 gm.) daily. Regardless of the type of preparation, some persons will show a sensitivity to iron salts, the commonest reaction being gastrointestinal irritation with gaseous distention, occasionally pain, and in some instances diarrhea or constipation. In some this reaction is so severe that therapy must be stopped. One way in which these reactions may be minimized is to start administration with only one 5 grain (0.3 gm.) tablet per day and increase to the full dose over a period of a week. By giving the iron with the meal, reaction may be avoided at times. To follow the response to iron, just as the response to treatment of pernicious anemia, the percentage of reticulated erythrocytes can be determined; the peak of the response comes between the 8th and 12th or 14th days after initiation of treatment.

Although dilute hydrochloric acid has been recommended for persons with achlorhydria who have not responded well to oral administration of iron, there is no clear-cut evidence to suggest that this substance increases the absorption of iron. A well-balanced diet with adequate high quality protein should, of course, be used. However, for iron deficiency anemia there is no recognized indication for the administration of liver extract (orally or parenterally), and the administration of the iron-liver-stomach combinations that are prescribed so commonly can serve only to increase the cost of medication without effecting regeneration of blood in any way except by their content of iron. With all the publicity given to medical subjects today, the patient knows that liver and stomach are used in treatment of the anemias. Lacking, however, the discernment necessary to dis-

2. Granick, S.: Iron Metabolism and Hemochromatosis, *Bull. New York Acad. Med.*, 45:403 (July) 1949.

3. Scott, J. M., and Govan, A. D. T.: Anaemia of Pregnancy Treated with Intravenous Iron, *Lancet* 1:367 (Feb. 17) 1951.

tinguish between the various types of anemia, the medical public is today being sold a bill of goods.

As already mentioned, the response of reticulated erythrocytes serves as an index of the response to therapy with iron. Too often iron therapy is continued for an indefinite period, sometimes extending over years without any improvement on the part of the patient. Often, too, iron is administered to women, particularly those who have hemoglobin within the limits of normal and who cannot be expected to give any response. For women who have anemia on the basis of simple menorrhagia and for whom no surgical procedure is indicated, the use of iron for an indefinite period to maintain normal values of hemoglobin is indicated, although such patients should be observed from time to time to be certain that no other pathologic conditions are developing.

When massive hemorrhage has caused depletion of stores of iron, it seems reasonable to continue the therapy with iron for a considerable period after the return to normal in order that reserves of iron may be returned to normal. As yet, sufficient data are not available to permit determination of the period of time required for restoration of such stores of iron.

Parenteral Administration.—A small percentage of patients who have an iron deficiency anemia, for one reason or another do not tolerate or respond to oral administration of iron. These include patients who may be sensitive to iron or who have severe gastrointestinal symptoms after its oral intake or who, according to some observers, fail to absorb iron. Within the past few years satisfactory preparations of saccharated iron oxide have been developed which can be administered intravenously with safety and to which there is gratifying response. Formerly the disadvantages of parenterally administered iron were the toxic reactions that occurred in many of these patients. The possibility of toxic accumulations of iron from long-continued administration has not been sufficiently explored for the possibility of serious end results to be excluded entirely. The tendency to substitute intravenous iron therapy at high cost for oral treatment at nominal expense for a large group of patients who can and will make a satisfactory response to iron given by mouth is undesirable and should be guarded against. English observers recently have questioned whether iron should ever be administered intravenously in doses of more than 100 mg. per injection.

Brown and associates⁴ have recently reported their experience with intravenous use of preparations of this kind. By a simple formula proposed by them, the amount of metallic iron can be easily calculated and allowance can be made in addition for iron storage depots. Injections can be given once or twice daily. My colleagues and I have followed the formula of allowing approximately 25 mg. of metallic iron for each 1% deficit in the hemoglobin. The response to this treatment can be followed by frequent determinations of the percentage of reticulated erythrocytes. The peak of the response occurs between the 6th and 12th days after treatment is instituted. The increase in the concentration of hemoglobin and subjective improvement, indicated by a feeling of general well-being, occur surprisingly rapidly. Reactions are mild and infrequent.

LIVER EXTRACT THERAPY

Since the introduction by Minot and Murphy⁵ of liver therapy for pernicious anemia, in 1926, many materials have been produced that have simplified for both the patient and the physician the treatment of this disease. Physicians sometimes lose sight of the fact, however, that the end result of treatment has not been improved on and that whole raw liver gave the patient the same beneficial result as the most potent liver extract on the market today. Just to refresh memories, I should like to mention some of the materials used in the past 25 years. Whole liver, raw or cooked, was soon followed by the production of fraction G of Cohn, the latter being given as an extract for oral use. Within a short time after the introduction of this extract and as a consequence of the work of Castle, desiccated hog stomach was utilized. This was followed by liver extracts for parenteral injection, so-called crude and refined, dilute and concentrated. For the past 18 to 20 years liver extracts for intramuscular use have dominated therapy; liver extracts for oral use, desiccated defatted hog stomach, or liver-stomach concentrates have contributed only a small amount to the total treatment of pernicious anemia. With this long period of use of liver extracts behind us, the present is an excellent time to evaluate what these preparations will do in control of the symptoms of pernicious anemia.

Parenteral Administration.—After the diagnosis of pernicious anemia has been firmly established, treatment can be reduced to a relatively simple formula by dividing the cases into (1) those in which anemia is the primary finding and in which there are no neurologic symptoms or findings and (2) those in which neurologic symptoms are present with or without anemia. For many years I have treated patients in group 1 by giving them intramuscularly 1 cc. of a 15-unit preparation daily for three days and then 1 cc. weekly until the erythrocyte count had reached a normal level. After this the interval between injections is gradually increased to three weeks, and then the patient is asked to have the hemoglobin checked and erythrocyte counts at intervals of four to six months. Patients are warned that a decrease in the value for hemoglobin and in the erythrocyte count or the appearance of glossitis, paresthesias, or diarrhea indicates inadequate treatment and that either the amount of injectable material should be increased or the interval between injections decreased. Likewise the patient is warned that active infections, such as pneumonia and infections of the urinary tract, require administration of increased amounts of liver extract as a rule.

For the patients in group 2 a somewhat different plan is outlined. In this group are patients who have varying degrees of neurologic involvement, from mild to extremely severe. When liver therapy was first introduced, the response of neurologic symptoms was not entirely satisfactory, until as a result of work done by Longcope and associates⁶ it was realized that two or three times

4. Brown, E. B.; Moore, C. V.; Reynafarje, C., and Smith, D. E.: Intravenously Administered Saccharated Iron Oxide in the Treatment of Hypochromic Anemia; Therapeutic Results, Potential Danger and Indications, *J. A. M. A.* 144: 1084 (Nov. 25) 1950.

5. Minot, G. R., and Murphy, W. P.: Treatment of Pernicious Anemia by a Special Diet, *J. A. M. A.* 87: 470 (Aug. 14) 1926.

6. Baker, B. M., Jr.; Bordley, J., III, and Longcope, W. T.: Effect of Liver and Liver Extract upon the Symptoms and Signs Referable to Nervous System in Pernicious Anemia, *Minnesota Med.* 13: 815 (Nov.) 1930.

the maintenance dose or even more had to be given to bring about satisfactory improvement. Thus, when the first extracts for parenteral injection were introduced, experience already had shown that hematologic maintenance doses would not be sufficient for the treatment of patients with neurologic manifestations of pernicious anemia. Therefore, treatment of these patients is started as is treatment of patients in group 1, that is, 1 cc. of a 15-unit preparation of potent liver extract is given daily for three days and then 1 cc. of a 15-unit preparation is given every five to seven days. The latter dose is continued for two months and then, as suggested by Strauss⁷ many years ago, the patient's condition is reconsidered. If the patient is making adequate progress, treatment is continued as in the initial plan; but, if the patient has not shown evidence of betterment, either the interval between injections is decreased or the amount of liver extract per injection is doubled. With many other observers my colleagues and I have found use of physical therapy and of coordinated exercises helpful adjuncts in the handling of this group of patients. The rapidity of improvement of patients in this group varies a great deal, and we have seen some patients who continued to improve for as long as 18 to 24 months after the initiation of therapy. A small group of patients will not obtain benefit, and the improvement of another small group will fall short of that which could be desired. We have not seen progression of symptoms occur in any patient receiving adequate therapy even though no improvement may be evident. Maintenance therapy in this entire group after either complete relief or after a prolonged period in which further improvement is not made should be carefully supervised.

For the past 20 years, we have not prescribed dilute hydrochloric acid for these patients. We have not been pressed at any time that patients with pernicious anemia have benefited by such administration and, as a matter of fact, seriously question whether dilute hydrochloric acid should be prescribed for any patient at any time.

Aside from what is advocated as a good adequate diet, no special vitamin supplements, including vitamins B₁ and C, have been prescribed for the treatment of pernicious anemia. Since for many years we have believed that patients with pernicious anemia are more susceptible to carcinoma of the stomach than the normal population, we have advocated yearly roentgenoscopic examination of the stomach and warned patients of the desirability of immediate roentgenoscopic examination if symptoms develop at any time in the interval between these examinations. Other competent observers in the field are at variance with this advice and recommend more frequent roentgenoscopic examinations. However, it has seemed to us that yearly examination is a practical approach, and in advising more frequent examination there is danger that the patient will avoid the examination entirely rather than submit to the expense of an examination the need for which it is difficult for him to understand.

The question is often asked: Is it feasible to teach patients to give their own liver extract, and do any difficulties result from self-administration? For the past 13 years we have offered all patients requiring regular treatment with liver extract the opportunity of learning how to give their own treatment. A small proportion of these patients prefer to have their injections given by someone else. However, the majority accept the opportunity of learning to give their own injections, and in so far as we have been able to observe these patients have not had any difficulty because of self-administration. Occasionally, contrary to our suggestion, we have patients who prefer to take extracts by mouth. Here we prescribe either a solution of liver extract or one of the desiccated stomach or liver-stomach preparations for use in pernicious anemia.

Not infrequently the question arises as to whether present-day methods of treatment of pernicious anemia are superior to those first used at the time of the introduction of liver. From the standpoint of actual clinical improvement and without consideration of other factors, there is no reason to believe that the results produced by adequate amounts of raw or cooked whole liver were in any way inferior to those produced by the most approved liver extracts or vitamin B₁₂ preparations. However, in other respects, liver extracts and vitamin B₁₂ preparations have many desirable advantages.

Although there is no uniformity of opinion among well-informed hematologists concerning the exact amount of liver extract to be used in a given case, it is generally agreed, however, that, although no harm results from excessive amounts of liver extract, no real good results from it.

VITAMIN B₁₂

In the years 1930 to 1947 much effort was expended in trying to isolate from liver the principle responsible for the beneficial results in pernicious anemia. Then, in 1948, essentially simultaneously, Smith and Parker⁸ in England and Rickes and co-workers⁹ in this country isolated in crystalline form the cobalt-containing substance now known as vitamin B₁₂. This is now obtainable as a solution of the pure crystalline material or as concentrates containing vitamin B₁₂ for parenteral use. The material is packaged on the basis of actual micrograms (0.001 mg.) in the solution of crystalline material or the equivalent in the concentrates, the latter values being established on the basis of microbiologic tests.

Vitamin B₁₂ must be given parenterally in order to obtain the maximal benefit for the minimal cost. With parenteral administration the response of reticulated erythrocytes and the increase in number of erythrocytes and concentration of hemoglobin are of the same general order and occur within essentially the same time limits as their response to parenteral use of potent liver extracts. In brief, clinical results from the use of adequate amounts of vitamin B₁₂ for pernicious anemia alone appear to be equal in every way to those obtained from a potent liver extract. There is, however, considerable variation in the amounts of crystalline B₁₂ believed by various observers to be necessary for adequate treatment. Although in our hands 15 µg twice a month has constituted adequate treatment for the patient with pernicious anemia alone, other observers recommend as

7. Strauss, M. B.: *The Pharmacopeia and the Physician; Use of Drugs in Treatment of Anemia*, J. A. M. A. **107**: 1633 (Nov. 14) 1936.

8. Smith, E. L., and Parker, L. F. J.: *Purification of Antipernicious Anemia Factor*, *Biochem. J.* **43**: viii, 1948.

9. Rickes, E. L., and others: *Crystalline Vitamin B₁₂*, *Science* **107**: 396 (April 16) 1948.

much as 80 μ g per month. Just as when liver extract is used, the patient with neurologic manifestations requires an increased amount. Although our experience with treatment of patients with neurologic manifestations of pernicious anemia does not permit us as yet to state unequivocally that vitamin B₁₂ will do everything potent liver extract will do, all the evidence at hand so far tends to substantiate such a viewpoint.

The use of crystalline B₁₂ does have certain advantages over use of liver extracts: (1) it can be used in instances of sensitivity to liver extract, and (2) it permits the use of specific quantities of purified crystalline preparations. Some manufacturers have placed on the label of their preparations of liver extract the approximate number of micrograms of vitamin B₁₂ contained per unit. Recent observations in England through the use of microbiologic tests, however, have shown that in some instances the number of micrograms per cubic centimeter reported was far greater than could be determined on the basis of these tests. Thus the second advantage is still applicable.

There are in the literature reports on the use of various analogues of B₁₂ in which there is only a slight change in the molecule or the addition of a simple chemical group. The preparations are known as vitamins B_{12A}, B_{12B}, B_{12C}, and B_{12D}. The response of the patient to these is essentially the same as with vitamin B₁₂.

Vitamin B₁₂ is reported effective in the treatment of fish-tapeworm anemia and the megaloblastic anemia of total gastrectomy. However, in one report of megaloblastic anemia in total gastrectomy there was only partial response to vitamin B₁₂, and it was only after the addition of folic acid that the hemoglobin and erythrocyte count returned to normal levels. In nutritional macrocytic anemia, sprue, megaloblastic anemia of intestinal disease, and megaloblastic anemia of infancy the results produced by vitamin B₁₂ have been variable.

Although most reports on treatment of megaloblastic anemia of pregnancy and the puerperium show failure of response to vitamin B₁₂, Patel and Kocher¹⁰ reported the successful treatment in Bombay of five patients with this type of anemia, by injection of 40 μ g of vitamin B₁₂. This is in direct contrast to the report of Ungley and Thompson,¹¹ who obtained no results with 65 to 80 μ g and then a response to 2.5 mg. daily of folic acid.

FOLIC ACID

Folic acid was first isolated in 1943 and synthesized in 1945. The property of being essential for the growth of *Lactobacillus casei* and *Streptococcus faecalis* R makes possible its reasonable quantitation through microbiologic assay. It is an essential factor for hemopoiesis in man, monkeys, and certain other species. Deficiency of folic acid produces megaloblastic erythropoiesis, and administration of folic acid results in a prompt conversion of such a blood picture back to one of normoblastic regeneration.

The commercial product is available as a 5 mg. tablet for oral use or in solution containing 15 mg. per cubic centimeter for parenteral administration. Since folic acid is readily absorbed from the gastrointestinal tract, parenteral administration ordinarily has no advantages.

For pernicious anemia the administration of folic acid while bringing about a satisfactory hematologic remission and conversion of the marrow from a megaloblastic to a normoblastic state is not considered to be adequate treatment, since eventually a certain number of these patients have hematologic relapse. Furthermore, in spite of what is apparently adequate administration of this substance, neurologic and gastrointestinal manifestations of the disease may progress or even develop when they have not been previously present. Therefore, while its administration for pernicious anemia is not contraindicated, its use is not warranted.

However, in the treatment of megaloblastic anemia of pregnancy and the puerperium, anemia associated with intestinal disease, such as strictures and fistulas, nutritional macrocytic anemia of the tropics, megaloblastic anemia of total gastrectomy, and sometimes of megaloblastic anemia of infancy, use of folic acid results in prompt and excellent recovery. In most of these conditions, except pernicious anemia, treatment may be discontinued after recovery of the patient from the anemia. Folic acid also is said to be of value in treatment of tropical sprue. Girdwood¹² questioned whether the tropical sprue of Spies is the same as that reported from the tropics by the English, and he stated that he preferred to think of Spies' cases as instances in which malnutrition plays a large role.

CITROVORUM FACTOR OR FOLINIC ACID

In 1948 Sauberlich and Baumann,¹³ while working with cultures of *Leuconostoc citrovorum*, found that for satisfactory growth a factor had to be added to the medium that was not present in the usual vitamin B complex. They found a good source of this growth factor in refined liver extracts used for treating pernicious anemia. This was termed "citrovorum factor." Bardos and others¹¹ found a substance effective in neutralizing the inhibiting action of methyl folic acid. They called this folinic acid and found it would act as growth factor for *Leuconostoc citrovorum*. In the citrovorum factor and folinic acid we are probably dealing with the same substance. This substance has been found capable of converting the megaloblastic marrow of pernicious anemia to a normoblastic one with adequate improvement in concentration of hemoglobin and number of erythrocytes. Experience with this substance is insufficient as yet for anyone to know whether it will merely react on a megaloblastic marrow and convert it to normal and then as in the case of folic acid fail to prevent gastrointestinal and neurologic manifestations and permit eventual relapse of hematologic symptoms. Our small experience confirms the good hematologic response reported recently by Davidson and Girdwood.¹⁵

10. Patel, J. C., and Kocher, B. R.: Vitamin B₁₂ in Macrocytic Anaemia of Pregnancy and the Puerperium, *Brit. M. J.* 1: 924 (April 22) 1950.

11. Ungley, C. C., and Thompson, R. B.: Vitamin B₁₂ and Folic Acid in Megaloblastic Anaemias of Pregnancy and the Puerperium, *Brit. M. J.* 1: 919 (April 22) 1950.

12. Girdwood, R. H.: Vitamin B₁₂ and Related Factors; a Clinical and Experimental Review, *Edinburgh M. J.* 57: 72 (Feb.) 1950.

13. Sauberlich, H. E., and Baumann, C. A.: A Factor Required for the Growth of *Leuconostoc Citrovorum*, *J. Biol. Chem.* 176: 165 (Oct.) 1948.

14. Bardos, T. J.; Bond, T. J.; Humphreys, J., and Shive, W.: Relationship of the Folinic Acid Group and the *Leuconostoc Citrovorum* Factors, letter to the editor, *J. Am. Chem. Soc.* 71: 3852 (Nov.) 1949.

15. Davidson, L. S. P., and Girdwood, R. H.: Treatment of Pernicious Anaemia with *Leuconostoc Citrovorum* Factor, *Lancet* 1: 722 (March 31) 1951.

SUMMARY AND COMMENT

Except possibly in some very unusual situation the treatment of anemia resolves itself into the use of specific substances depending on the morphologic blood picture. In hypochromic anemias, which are usually due to loss of blood, the proper treatment is the oral use of a preparation of iron. For these anemias, liver extract, vitamin B₁₂, folic acid, desiccated hog stomach, and stomach-liver or iron-stomach-liver preparations serve no useful purpose and are definitely not indicated. In those unusual instances in which iron taken by mouth cannot be tolerated or produces an increase in gastrointestinal symptoms, it can be given intravenously.

The commonest diagnosis of macrocytic anemias with megoblastic type of bone marrow in northern United States is pernicious anemia. The most desirable form of treatment of this type of anemia is the parenteral use of a potent liver extract or the parenteral use of vitamin B₁₂. Preparations of liver or stomach or liver-stomach combinations for oral administration can be used and are effective when given in adequate amounts. The presence of neurologic manifestations with pernicious anemia requires that much larger quantities of potent material be used either parenterally or orally. Iron is not indicated unless loss of blood is associated with pernicious anemia. Folic acid, while not contraindicated, is not necessary in the complete treatment of pernicious anemia and, when used alone, constitutes inadequate treatment.

Concerning other diseases associated with megaloblastic anemia, there are differences of opinion regarding the response to vitamin B₁₂ and folic acid. Some patients will respond only partially or not at all to vitamin B₁₂, and subsequently a good result can be obtained with folic acid. Many of the anemias in this group have to be treated on a trial and error basis, since with our present knowledge we have no way of knowing which material is going to be effective.

None of the substances discussed in this paper are of value in the treatment of the anemia associated with (1) various types of malignant lesions, particularly those with metastasis to the bone marrow, (2) diseases of the reticuloendothelial system, such as the various leukemias and aplastic anemia, and (3) diseases in which there is toxemia or interference with metabolism of hemoglobin such as is seen in chronic glomerulonephritis with azotemia or in infections. In rheumatoid arthritis oral administration of iron is of no benefit, and the experience with iron given intravenously is as yet too limited to permit a satisfactory opinion.

Treatment with iron, liver extract, vitamin B₁₂, and folic acid is of benefit only when these substances are deficient, and none of these forms of medication is helpful in anemia due to some cause other than that produced by these specific deficiencies. A useful maxim then is: Determine the type of anemia present, give only the medicament indicated; do not mix the treatment.

MANAGEMENT OF BREECH PRESENTATION IN PREGNANCY AND LABOR

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and

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Evidence that the management of breech presentation in pregnancy and labor is a controversial issue continues to appear.¹ Much has been written on the subject stressing the higher natal and neonatal mortality and the greater incidence of morbidity and injury to both the mother and baby attending this manner of birth. The prophylactic value of external cephalic version late in pregnancy is generally recognized, and there is manifest a definite trend of opinion favoring a partly spontaneous rather than a completely artificial termination of the second stage of labor.

Statistics show that a low fetal mortality is attainable provided the attendant observes certain fundamental and

recognized principles peculiar to breech delivery, allow ample time for maximum dilatation of the cervix, and does not attempt delivery from below if borderline positive cephalopelvic disproportion exists.

It is the purpose of this paper (1) to show the reduction in the incidence of breech presentation in labor that can be accomplished by external version late in pregnancy; (2) to show the reduction in fetal mortality and morbidity that is obtainable by conservative management, i. e., limiting total extraction to only those cases in which spontaneous bulging or crowning fails to occur; and (3) to emphasize the essential manipulations employed to minimize fetal mortality and morbidity. Emphasis is to be placed on the element of fetal risk concerned with the timing and technique of breech delivery itself.

MATERIAL

The analysis is based on a review of all breech deliveries occurring in 7,433 consecutive private cases, each delivery having been attended by some member of our group.

Statistics of fetal mortality show great variance among writers on this subject, owing mainly to the lack of a standard to follow in the elimination of factors that influence fetal risks. For example, Moore and Steptoe² and Patton and Mussey³ include fetal weight of 1,500 gm. or more, Gordon⁴ uses fetal weight of 2,500 gm. or more, and Hansen⁵ includes all weights, in present

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1. Ward, S. V., and Sellers, T. B.: Controversial Issues in Breech Presentation, *South. M. J.* 43: 879-886, 1950.

2. Moore, W. T., and Steptoe, P. P., Jr.: The Experience of the Johns Hopkins Hospital with Breech Presentation: An Analysis of 1,444 Cases, *South. M. J.* 36: 295-303, 1943.

3. Patton, G. D., and Mussey, R. D.: Breech Presentation: A Study of 292 Cases, *Proc. Staff Meet., Mayo Clin.* 15: 389-393, 1940.

4. Gordon, C. A.; Garlick, R., and Ogniz, P.: An Analysis of 3,301 Breech Deliveries in the Hospitals of Brooklyn, New York, *Am. J. Obst. & Gynec.* 28: 140-150, 1934.

5. Hansen, E. M.: Breech Delivery, *Am. J. Obst. & Gynec.* 41: 575-582, 1941.

ing mortality results. Guyer,⁶ Goethals,⁷ and Greig⁸ exclude cases of prolapse of the cord, whereas Seeley⁹ and Potter¹⁰ feel that this complication cannot be eliminated in arriving at a corrected fetal loss. In order to fairly attribute natal and neonatal mortality and morbidity to only those factors peculiar to breech delivery, it is believed proper to exclude those cases in which other conditions affecting the mother or baby might contribute to an unfavorable outcome.

We have therefore excluded all babies weighing less than 6 lb. (2,722 gm.). Babies weighing less than this seldom present serious difficulties in delivery, but, owing to the small presenting part, prolapse of the cord is a more frequent complication and neonatal death is due more to prematurity than to the effects of breech delivery.

In addition to limitation of underweight, it was considered justifiable to exclude other fetal handicaps, such as hydramnios, erythroblastosis, and gross malformations. Prolapse of the cord, if present on admission to the hospital or before the cervix was dilated sufficiently to permit delivery, was also excluded. Likewise, exception was made if the fetal heart beat was unobtainable on admission.

Maternal complications detrimental to the baby, such as placenta previa, abruptio, pre-eclampsia and eclampsia, chronic nephritis, syphilis, diabetes, and severe cardiac disease, justified exclusion of the case. Multiple pregnancy was excluded, since inertia, hydramnios, and interference with manipulations and the normal mechanism of labor are uncontrollable factors.

There were 193 breech deliveries among 7,433 consecutive cases reviewed, an incidence of 2.6%. With the omission of 46 cases in which the fetal weight was less than 6 lb. (2,722 gm.) and three cases in which macerated babies were delivered, there remained 144 cases, an incidence of 1.9% of term breech deliveries, for analysis.

MANAGEMENT OF BREECH PRESENTATION IN PREGNANCY

It is generally agreed that conversion of breech to cephalic presentation late in pregnancy is a worth-while procedure in reducing the incidence of breech presentation in labor and thereby lowering fetal mortality and morbidity. For many years one of us (R. A. B.) has practiced and taught the value of this procedure.¹¹ Ryder¹² in 1942 reported 92.5% success in performing external version and showed an incidence of 2% breech delivery in 1,700 consecutive viable cases. Eastman¹³ states, "The procedure, if properly and gently performed, carries little danger, although not as much is accomplished by it as might be supposed." From a thorough review of the literature in 1949, Seeley⁹ stated that 17 of 21 authors recommend this procedure as a valuable aid in reducing the incidence of breech delivery. Hanley¹⁴ stated that the procedure is dangerous because of the uncertainty of the location of the placenta, and Trites¹⁵ said, "The hazards of breech delivery are not sufficiently great to justify too vigorous or persistent attempts at external version."

Breech presentation was observed 2,251 times in 1,438 consecutive patients during routine abdominal examination from the sixth month of pregnancy to delivery. There were 624 nulliparas, among whom breech presentation was observed 1,048 times, and 814 multiparas, among whom there were 1,203 instances of this presentation. Considering the infrequency of prenatal visits and probability of frequent spontaneous changes in presentation, this figure grossly understates the actual occurrence of breech presentation in the last trimester of pregnancy.

External version was attempted 1,161 times and was successfully performed in 64.4%. At subsequent exam-

inations the presentation was noted to have reverted to breech in 19.1%. In 118 instances external version failed with one attempt; in 86 instances with two attempts, and in 209 instances with three or more attempts.

As might be expected there was a higher incidence of successful external version in multiparas (77.9%) than in nulliparas (50.7%); likewise there was a higher incidence of reversion to breech in multiparas (20.7%) than in nulliparas (16.6%).

Figure 1 shows the percentage of success and failure attending the operation of external version, from breech to cephalic, at successive stages of pregnancy from the sixth calendar month to and shortly beyond the ninth month of pregnancy. It also shows the per cent of observed reversions, cephalic to breech at the same specified periods. During the seventh month, 84.7% of the attempted external versions were successful. The unexpectedly low incidence (2.1%) of spontaneous reversion is obviously explained by the infrequent observations at this stage. Many unobserved spontaneous versions and reversions must have taken place during this period.

There follows a progressive decrease in successful external versions until term or shortly beyond, when there is an unexpected increase, probably owing to more in-

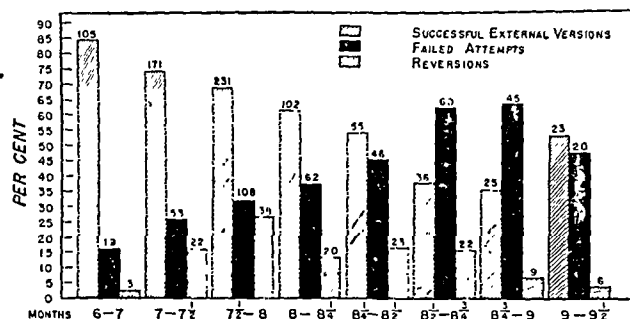


Fig. 1.—Chart showing 748 successful external versions, 413 failed attempts, and 143 reversions at successive stages of pregnancy.

tensive effort at this late stage. The percentage of spontaneous reversion lessens as term is reached.

Since many breech presentations correct themselves spontaneously, it is of interest to analyze the total number of breech presentations in this category. Spontaneous version occurred 778 times among 2,251 observed breech presentations. Sixty-eight of these followed a failed external version. The total number of spontane-

6. Guyer, H. B., and Heaton, C. E.: The Fetal Risk in Breech Delivery: A Study Based on 708 Cases, *Am. J. Obst. & Gynec.* 52: 362-371, 1946.

7. Goethals, T. R.: Management of Breech Delivery in Primiparas, *Am. J. Obst. & Gynec.* 37: 663-674, 1939; Management of Breech Delivery in Multiparas, *ibid.* 38: 105-111, 1939.

8. Greig, D. S.: The Uncomplicated Primigravid Breech: Technique Used in Series of 60 Cases, *J. Obst. & Gynaec. Brit. Emp.* 52: 122-129, 1945.

9. Seeley, W. F.: Fetal Mortality in Breech Deliveries, *Am. J. Obst. & Gynec.* 57: 113-124, 1949.

10. Potter, M. G.; Erving, H. W., and Brown, J. B.: Observations on Breech Deliveries in General Hospital, *Am. J. Obst. & Gynec.* 49: 567-575, 1945.

11. Bartholomew, R. A.: Prophylactic External Version, *Am. J. Obst. & Gynec.* 5: 648-660, 1927.

12. Ryder, G. H.: Breech Presentations Treated by Cephalic Versions in the Consecutive Deliveries of 1,700 Women, *Am. J. Obst. & Gynec.* 45: 1004-1025, 1943.

13. Eastman, N. J.: Williams Obstetrics, ed. 10, New York, Appleton-Century-Crofts, Inc., 1950.

14. Hanley, B. J., and Rosenblum, G.: Breech Delivery: Review of 218 Cases, *West. J. Surg.* 45: 98-104, 1937.

15. Trites, A. E.: A Study of Breech Delivery, *Am. J. Obst. & Gynec.* 55: 430-436, 1948.

ous versions would, no doubt, have been greater had not routine external version been practiced. It is evident that spontaneous version (breech to cephalic) occurs most frequently from the sixth to the end of the eighth month, after which it occurs less frequently and declines less rapidly.

As shown in figure 2 the total number of reversions from cephalic to breech following spontaneous version increases from the sixth to the end of the eighth month but diminishes near term. The highest incidence of reversion, whether after external version or after spontaneous version, was in the period from seven and one-half to eight months. Spontaneous version may occur occasionally at or beyond term, when the attendant has desisted from further efforts to perform external version.

Reversion to breech presentation after external version occurs with greater frequency than after spontaneous version. This has been mentioned by many writers. In 748 successful external versions in our series, reversion occurred in 19.1%, whereas, in 778 spontaneous versions, reversion occurred in only 9.6%.

Some doubt has been expressed as to the actual benefit of external version in reducing the incidence of

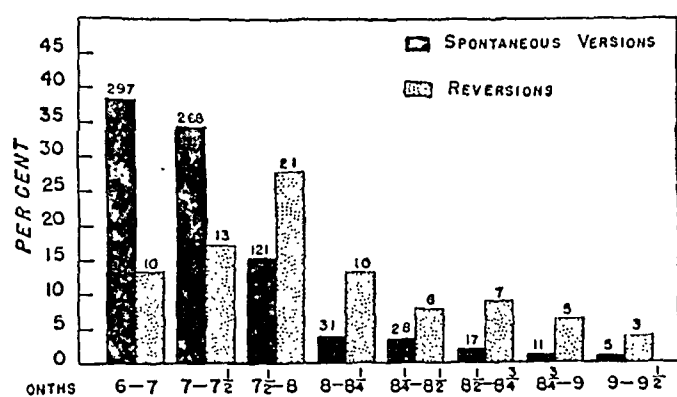


Fig. 2.—Chart showing 778 spontaneous versions and 75 reversions at successive stages of pregnancy.

breech delivery, which is generally considered to be 3% to 4% of babies born from seven months to term. In our series, with routine external version, there was an incidence of 2.6% breech deliveries, on the above basis, but, if one considers only full term babies weighing 6 lb. (2,722 gm.) or more, which, by reason of their size, encounter greater hazards if delivered as breech, the incidence is reduced to 1.9%. If one accepts as a conservative estimate an over-all fetal mortality of 10% for breech delivery, the fetal salvage is worth while, but, for those whose management of breech delivery is attended by a very low mortality, the fetal salvage effected by routine external version would seem to be negligible. However, since there was no recognizable harm to the mother or baby in 1,161 attempted external versions, successful and unsuccessful, there can be no objection raised to employment of this procedure. There was very little discomfort to the patient during or after the performance of external version, and in many instances a feeling of greater comfort was expressed by the patient following this procedure.

As to the optimum stage of pregnancy for first employment of external version, we have long felt that breech presentation in the nullipara should be ignored until pregnancy has reached seven and one-half calendar

months, and in the multipara, eight months. The impression was held that prior to these stages recurrence of breech presentation was too frequent, but further postponement involved greater difficulty in turning the baby. This impression is apparently borne out in both external and spontaneous version at seven and one-half to eight months (fig. 1 and 2). On the contrary, Ryder advocates external version at any time a breech presentation is found.

TECHNIQUE OF EXTERNAL VERSION

The first essential point in the technique of performing external version should be gentleness in palpation. The patient should be relaxed and the bladder empty, and there must be an accurate preliminary diagnosis of presentation and position. The breech is first raised from the pelvis with both hands and carried toward the lower quadrant opposite to that toward which the head is to be brought down. If the breech is engaged at one visit, it is important to re-examine the patient in one week, when the breech may be found disengaged and movable. The attitude of flexion is maintained by pushing down with one hand on the fetal head while the breech is pushed toward the fundus with the other, using the flat of the fingers and exerting gradual and intermittent pressure. One is probably less likely to disturb the placental site if more effort is exerted in pushing the breech up than pushing the head down. It is important to rest the patient at intervals, take ample time, but continue support to the breech to avoid losing any of the gain made. During this short rest the baby may kick against the hand supporting the breech and thereby accomplish the turn.

It is not necessary to stop the maneuver to listen to the fetal heart from time to time, since slowing of the heart rate is apparently due to pressure on the head and not on the cord, as was first affirmed by Kautsky (in Eastman¹³).

If external version proves too difficult, it is far better to desist and try again after an interval of one week than to use too much force. Owing to the temptation to use too much force, anesthesia is not justifiable, except perhaps in borderline cephalopelvic disproportion, in which a test of labor is desirable, or in a case of transverse presentation on admission of the patient in labor. Usually the operation is successful if it is possible to move the fetus from breech to a transverse position.

After successful external version it is best to rest the patient a few minutes, then try to settle the fetal head into the pelvic inlet and fix it manually by the use of fundal or suprapubic pressure. It is advisable to see the patient one week after successful version, in order to determine whether reversion has occurred. If the version is unsuccessful near term and a breech delivery is necessary, the patient should be advised to enter the hospital early in labor, to afford better opportunity to preserve the membranes and, in the event of early spontaneous rupture, to permit quick determination of the possibility of cord prolapse. On account of the increased fetal mortality with large babies, one should allow not over 10 days to two weeks overtime, provided the patient presents findings favorable for induction, such as descent of the breech and an effaced dilating cervix,

Induction of labor prior to this is contraindicated, for the convenience of the patient or the doctor, because of the well-known hazards of inertia and poor dilatation of the cervix that might follow.

MANAGEMENT DURING LABOR

When labor reaches the stage at which the breech is at or below the spines, the cervix may seem to be fully dilated, but actually it may not be dilated sufficiently to pass the head. This false interpretation is particularly true of footling and complete breech but less so of frank breech, in which variety the presenting part is larger and effects more dilatation, being made up of the thighs and lower part of the trunk.

It is at this point that the attendant may be tempted to undertake extraction or may choose to follow a routine practice of breaking up a full or frank breech that has progressed to bulging but not crowning. It is this practice that is generally believed to be unwise and should not be employed unless the patient fails to advance the breech to crowning of the anterior hip and appearance of the anus over the perineum after a further period of good labor. The object of this further test is to assure the maximum possible degree of dilatation of the cervix by the time spontaneous crowning occurs or when the patient has failed to make additional progress for one to one and one-half hours of good labor.

It appears that an analogy has been assumed between the common practice of prophylactic low forceps delivery in cephalic presentation and the feasibility of an early breaking up and extraction of complete or frank breech presentation. The analogy, however, does not hold true.

In cephalic presentation, the cervix is pushed down with the head and a state of full dilatation can be readily determined. The largest part of the baby is coming first, and a safe delivery is almost assured if the attendant is reasonably experienced in the use of forceps. In breech presentation, however, even though the attendant may be skilled in the performance of extraction, there may still be present some degree of cervical resistance which may delay delivery of the head and cause asphyxia of the baby.

If the head is held by the cervix, it is extremely difficult, if not impossible, to cut the cervix, as can be done in cephalic presentation, since the bulk of the fetal body in the vagina interferes. The same holds true should the arms become extended. It has been stated that the attendant may determine, by vaginal examination preceding extraction, that the cervix is not completely dilated, and, if not, he may manually complete the dilatation. This, also, would seem to be impossible for the reason stated above, plus the fact that very few cervices can be successfully dilated manually, even if the vagina is empty.

Furthermore, in frank breech presentation it is necessary to elevate the breech to successfully perform a Pinard maneuver. When the foot has dropped into the operator's hand, considerable elevation of the breech is also required to permit the thigh to pass through the arc necessary to pull the leg down. If ample elevation of the entire breech is obtained, there is danger of possible prolapse of the cord; if elevation is insufficient,

there may be overstretching of the lower uterine segment and danger of uterine rupture. Also the movements of elevating and then lowering the breech may extend the arms or predispose to nuchal hitch, which may delay delivery.

REQUIRED VERSUS ELECTIVE BREECH EXTRACTION

Complete breech extraction, as defined by Eastman,¹³ should therefore be qualified as to whether the operation is required or elective.

In the elective type the attendant assumes that the cervix is fully dilated and attempts to deliver by complete extraction. The patient may not have accomplished all the dilatation and descent of which she is capable, and with further test she might have been able to reach the stage of bulging and crowning. Full dilatation for the breech does not necessarily mean full dilatation for the aftercoming head. Further waiting would not have necessitated more than partial breech extraction to effect delivery.

In the required type of total breech extraction, the patient has made all the progress of which she is capable and there has been no advance for one to one and one-half hours. Failure to progress after an adequate test, therefore, constitutes an indication for a required total extraction. Assumption that the cervix is fully dilated is less likely to be in error in this case, since an ample test has been permitted.

The relative merits of assisted and complete breech extraction as to fetal mortality and injuries are strikingly shown in the summaries given by Gordon,⁴ Goethals,⁷ and Moore,² who have analyzed large series of cases according to the method of delivery. "Partial breech extraction" is the term proposed by Eastman, Greenhill, and McCormick (in Eastman¹³) to take the place of the term "assisted breech delivery." "Total breech extraction" is proposed to take the place of the term "extraction," and it is in this variety there arises the need of differentiating between "elective" and "required total breech extraction."

Gordon, excluding the same fetal and maternal extraneous factors as mentioned in our series, but choosing a fetal weight above 5½ lb. (2,495 gm.) rather than 6 lb. (2,722 gm.), showed the following results in 2,601 breech deliveries: in spontaneous or assisted breech delivery, the fetal mortality was 6.7% with an incidence of 2% fetal injury; in breeches extracted, the fetal mortality was 18.7% with 5% fetal injury; when the breech was "broken up" and extracted, the fetal mortality was 28.9% with 9.9% fetal injury.

Goethals, with the same fetal and maternal criteria as in our series and a fetal weight of 6 lb., obtained the following results in 500 pelvic deliveries of term breech presentations in nulliparas: Comparing the fetal mortality in this group during the first 33 years, when the policy at the Boston Lying-in Hospital was strict conservatism, with the last seven years, when the policy was changed to include "extraction with full dilatation," he showed a reduction in fetal mortality from 11% to 7.4%. However, in both periods alike, when the fetal loss was grouped into four types of delivery, "extraction with dilatation" showed the highest mortality.

Moore and Steptoe, using the same criteria but specifying a fetal weight of 5½ lb., studied the results in 1,444 breech deliveries, covering a 46-year period at the Johns Hopkins Hospital. A total mortality of 12.8% was found. The fetal loss was three times greater in the group of "decomposition and extraction" than in that of

TABLE 1.—Management of Term Breech Delivery in 144 Cases with Fetal Weight of 2,722 Gm. or More

Type of Delivery	Number	%
Cesarean section	14	9.72
Breech delivery	130	90.28
Spontaneous	0	0
Partial extraction	101	77.69
Total extraction	29	22.31
Required	16	55.17
Elective	13	44.83

"spontaneous to the umbilicus, then assist," during a period covering the first 36 years of this analysis. The highest fetal mortality of the last 10 years occurred among multiparas who were delivered by the method of "decomposition and extraction." The results obtained by those of lesser skill and experience who attempt to emulate these practices must inevitably be much more unfavorable.

Many of these patients were delivered by residents in training; hence the results would not be expected to equal those of long-experienced specialists. For example, Hansen,⁵ reporting 126 breech deliveries in 12 years of private practice, shows a corrected fetal mortality of 0.8%; Gustafson¹⁶ reported the loss of one baby in a series of 109 cases, and Greig⁸ showed one stillbirth occurring among 60 breech deliveries in nulliparas.

Skill and experience may compensate to some extent for ill-timed total elective extraction, but even in the best of hands there is a higher incidence of fetal mortality and morbidity than in cases of partial extraction.

In 16 of the 144 cases of term breech delivery, total extraction was required because of lack of progress in the second stage of labor, with the breech failing to advance to more than bulging or slight crowning for one to one and one-half hours. That the remaining 13 patients were delivered by elective total extraction, not in accord with the policy of expectancy which we advocate, was due in part to one of the group formerly favoring earlier interference.

TABLE 2.—Fetal Mortality

Type of Delivery	Total Cases	Mortality			
		Uncorrected		Corrected*	
		No.	%	No.	%
Spontaneous	0	..		..	
Partial extraction	101	3	2.97	1	0.69
Total extraction	29	4	13.79	0	0
Cesarean section	14	0		..	
Total	144	7	4.86	1	0.69

* Total corrected fetal mortality, excluding cesarean sections, 0.77%.

Table 2 shows the results obtained by favoring a policy of restricting total breech extraction to complete extraction of the "required" type.

A total of seven babies was lost, giving a gross mortality of 4.86%, which, after correction, is reduced to

0.69%. Excluding the cesarean sections, which carried no fetal mortality, the gross fetal mortality was 5.39%, corrected to 0.77%.

Cesarean section was performed in 14 cases. In five of these it was deemed advisable on account of a previous section. The indications in the remaining nine cases are recorded in Table 4. Two-thirds of these patients were over 30. One-third were nulliparas over 30.

Other data of interest in the 130 patients delivered through the pelvis may be mentioned as follows: Thir-

TABLE 3.—Causes of Fetal Mortality in 130 Breech Deliveries

Type Delivery	Stillbirth	Neonatal Deaths	Total	
Partial extraction	0	Erythroblastosis § Spina bifida; hydrocephalus Atelectasis ¶	Uncor- rected	Cor- rected
Total extraction (required)	Asphyxia-abruption placenta * Asphyxia; contraction ring; cervix 4-5 cm.†	0	2	0
Total extraction (elective)	Asphyxia-prolapsed cord; hydramnios; cervix 3 cm.‡	Pneumococcal meningitis; premature rupture of membrane §	2	0
			7	1

* Asphyxia: frank breech; total (required) extraction; weight 8 lb., 2 oz. (3,685 gm.); nullipara; failed version; spontaneous version at 8¼ months; reverted; onset of labor at 9½ months; premature separation of placenta.

† Asphyxia-contraction ring: frank breech; total (required) extraction; weight 6 lb., 6½ oz. (2,936 gm.); multipara; cessation of fetal heart when cervix was 4 cm. dilated; Bandl's contraction ring encircling fetus on undertaking delivery-craniotomy.

‡ Asphyxia-prolapsed cord: frank breech; total (elective) extraction; weight 7 lb., 14½ oz. (3,586 gm.); multipara; marked hydramnios; spontaneous rupture of membranes with rupture of marginal sinus of the placenta and hemorrhage; prolapse of cord through 3 cm. dilated cervix and rapid disappearance of fetal heart tones following insertion of bag.

§ Erythroblastosis: frank breech; partial extraction; weight 7 lb., 13 oz. (3,544 gm.); nullipara; transfusion 15 years previously; no difficulty with delivery; replacement transfusions; died on third day.

|| Spina bifida, moderate hydrocephalus: frank breech; partial extraction; weight 8 lb., 1 oz. (3,657 gm.); nullipara; failed external version; died on sixth day.

¶ Atelectasis, clinically: frank breech; partial extraction; weight 6 lb., 6½ oz. (2,892 gm.); multipara; premature rupture of membranes; precipitous labor; difficult to resuscitate; lived 4 days; lumbar puncture negative for blood; no autopsy.

§ Pneumococcal meningitis: frank breech; total (elective) extraction; weight 6 lb., 6½ oz. (2,936 gm.); multipara; premature spontaneous rupture of membranes 12 hours before onset of labor; uneventful delivery; lived 38 hours; autopsy.

TABLE 4.—Cesarean Section in 144 Term Breech Deliveries

	No.	Maternal Mortality	Fetal Mortality
Repeat	5	0	0
Primary	9	0	0

INDICATIONS FOR PRIMARY CESAREAN SECTION

1. Premature rupture of membranes; failure of dilation and descent.
2. Mid and outlet contraction of pelvis; inertia.
3. Nullipara; age 42; fibroid uterus; contracted outlet.
4. Insistence on live uninjured baby; liability of forelying cord (proved).
5. Suspected acute abdomen at term; risk of induction.
6. Nullipara; age 37; overdue; large baby; inertia after induction.
7. Age 36; previous difficult forceps; outlet contraction; insure healthy baby.
8. Age 39; para 2; no living children; insistence on healthy baby.
9. Funnel pelvis.

teen were in the age group 35-45 years, 82 were nulliparas, and 48 multiparas. The membranes ruptured spontaneously during labor in 59, prematurely in 44, and artificially in 27 cases. Labor began spontaneously in 116 and by induction in 14 cases. The breech was of the frank variety in 103 and incomplete in 27 cases. Episiotomy was performed in 122 cases; forceps were applied to the aftercoming head in 95 cases; a Pinard maneuver was done in 24 of the 29 total extractions. Seventeen patients had had previous breech deliveries. There were three cases (2.3% incidence) of prolapse of the cord, one of which accounted for a fetal death.

16. Gustafson, G. W.: Management of Breech Presentation, J. Indiana M. A. 42: 783-787, 1949.

Fetal injury occurred in four cases, or 3%, as follows: intracranial hemorrhage with convulsions and recovery; depression of the parietal bones bilaterally, as a result of slipping of Piper's forceps; fracture of the clavicle with the delivery of a nuchal arm; and one brachial plexus injury. The last two fetal injuries mentioned occurred when the total extraction was elective.

ESSENTIALS IN MANAGEMENT OF TOTAL BREECH EXTRACTION

Complete anesthesia is necessary in order that the attendant may be unhindered in his manipulations and maximum relaxation obtained. The anesthesia should be complete when extraction is undertaken. It is essential that the patient's legs be in stirrups or her hips to the edge of the bed and the legs supported. The bladder should be emptied.

Preparations should be made in advance for resuscitation of the baby—oxygen, tracheal catheter, bulb for aspiration of mucus, and hot blankets. Forceps should be in readiness for delivery of the aftercoming head, along with a retractor to depress the perineum to permit access of air, should the baby attempt to breathe before complete delivery.

After thorough ironing out of the lower vagina and perineum, with liberal use of medicinal soft soap solution, a deep mediolateral episiotomy should be done in all nulliparas just preceding extraction, to facilitate delivery and prevent tears through the rectal sphincter or anterior rectal wall. The same precaution applies to multiparas, but to a lesser degree.

To perform a Pinard maneuver, there should be ample elevation of the breech; the foot corresponding to the anterior leg should be grasped to favor keeping the back to the front, the other leg being released by flexion, when visible, pressing behind the knee. Towels aid one to maintain a secure hold on the advancing parts, and, when the umbilicus appears, a loop of cord should be pulled down to prevent stretching, since at this stage the cord may be compressed against the inlet.

The back is kept obliquely toward the front; the scapulas are brought well into view; the baby is depressed and the posterior shoulder rotated anteriorly toward the symphysis, by which maneuver the shoulder and arm come into view and are usually freed with ease. By reverse rotation, the other shoulder, which is now posterior, is brought anteriorly and released along with the arm, in the same manner, as described by Potter.

The head, which now comes into the pelvis (obliquely if the latter is normal, more in the transverse if contracted anteroposteriorly, or in the anteroposterior if the pelvis is narrow or of the male type) is guided and pressed down by the hand over the symphysis. Forceps should always be used to deliver the head if the patient is nulliparous, to prevent overstretching of the articulations of the cervical vertebrae, or of the brachial plexus if the attendant attempts delivery by downward pressure of the fingers placed on the shoulders. If the patient is multiparous, the same applies if manual efforts meet with undue resistance.

The delivery of the aftercoming head can be entrusted to the ordinary forceps, which in our experience have proved adequate. The head should first be brought

into the pelvis by manual manipulation from above and below, and the forceps are easily applied to the sides of the head in the mento-occipital diameter, when the chin is in view posteriorly. If the head is caught at the inlet, a specially designed forceps may reach to a higher level in the pelvis, but an application is difficult to secure. Owing to the greater spring in the long shanks of the Piper forceps, they may slip and groove the sides of the head, as happened in one case in our series. Once the chin and mouth are over the perineum and the baby has access to air, the head should be delivered very slowly, to lessen the risk of laceration of the rectal sphincter or anterior rectal wall.

In complete or frank breech, if impaction prevents delivery the breech must be elevated sufficiently to permit the feet and legs to be drawn down. In footling presentation, with one or both feet crowning and advancing rapidly, the feet may be wrapped in a sterile towel and held back until the patient is under anesthesia, prepared and ready for delivery. It is in these cases that the cervix may be even more inadequately dilated, because of the smaller bulk of the presenting part and seriously delayed delivery of the head.

Should there be difficulty in delivering an arm because of a nuchal hitch, one may try rotating the corresponding shoulder toward the hitch (hoping the arm will be displaced by friction) from behind the occiput toward the baby's face. If this fails, the breech is pushed up to elevate and loosen the arm, after which it may be reached and splinted down across the chest. In all maneuvers it is important to avoid excessive haste.

Finally, the baby should be thoroughly examined for injuries or evidence of spasticity, the perineum and vagina for extension of the episiotomy, the cervix for lacerations, and the lower uterine segment for possible tears.

CONCLUSIONS

1. By prophylactic external cephalic version, it was found possible to lower the incidence of breech delivery in the period of viability from the generally accepted frequency of 3.3% to 2.6% and for term breech delivery to 1.9% in 7,433 consecutive cases taken from private practice.

2. Total breech extraction should be qualified according to whether it is elective, on the assumption that the cervix is fully dilated and delivery feasible, or required, after an adequate test of labor gives more assurance that the cervix has attained maximum dilatation but the patient has ceased to make progress.

3. By limiting total breech extraction to only those cases in which bulging and crowning fail to occur spontaneously after an adequate period of good labor and by excluding those cases in which certain maternal and fetal complications involve risks to the baby, unrelated to breech delivery, it is possible to attain a fetal mortality rate comparable to that of cephalic presentation.

4. The uncorrected fetal mortality, natal and neonatal, was 4.8% and the corrected mortality 0.6%, cesarean sections included. The maternal mortality was nil.

5. The incidence of cesarean section was 9.7%; excluding the repeat sections, the incidence was 6.2%.

FACTORS IN THE ONSET OF CORONARY OCCLUSION AND CORONARY INSUFFICIENCY

EFFORT, OCCUPATION, TRAUMA, AND EMOTION

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Diseases of the heart, particularly those involving the coronary arteries, are the major medical problem facing us today. Estimates of the number of persons with heart disease in this country have varied up to eight million,¹ and practically half of cardiac deaths are caused by coronary artery disease.² We have estimated that one-half to one million attacks of coronary occlusion occur annually.³ Probably an equal number of acute coronary insufficiency occur.⁴ As the span of life has lengthened, the incidence of coronary artery disease has increased, and will continue to do so. It has been estimated that in 1980 there will be 42 million persons between the ages of 50 and 74—almost double the number in 1940.⁵

The importance of coronary artery disease in industry scarcely requires emphasis, considering that over 60 million persons are employed and that, although two-thirds of acute coronary attacks occur in persons over the age of 50, the disease is common in the fifth, and even in the fourth, decade.⁶ Accordingly, the question of the relationship of acute coronary episodes to effort and trauma has assumed paramount importance.⁷ It is now generally accepted that the vast majority of attacks of acute coronary occlusion take place fortuitously and spontaneously; the frequent occurrence during sleep is legendary. However, there is some disagreement in regard to the small group of cases in which an attack directly follows effort or trauma.⁸ We believe that much of this difference of opinion results from a confusion in terminology and would be dispelled if it were clearly realized that there are two types of acute coronary disease, i. e., acute coronary occlusion and acute coronary insufficiency, which usually differ in onset as well as pathologically and electrocardiographically.⁹ From the standpoint of therapy and compensability, it is essential to differentiate these two types of acute coronary episodes, even though they may simulate each other clinically. Not infrequently, coronary occlusion is said to have been caused by effort when actually study of the electrocardiogram discloses coronary insufficiency.¹⁰ In our experience coronary occlusion and coronary insufficiency present typical electrocardiographic patterns which differentiate them in 95% of the cases.

ACUTE CORONARY OCCLUSION

Acute coronary occlusion is a more or less rapid obstruction of a medium-sized or large artery by a thrombus, which usually results in a large, confluent, through-and-through infarct unless the patient succumbs very

early. The thrombus forms only in a previously sclerotic artery, either directly on an arteriosclerotic plaque or secondary to an intimal hemorrhage in such a plaque. In rare instances the hemorrhage forms a hematoma large enough to occlude the lumen without a thrombus.¹¹ Since the infarction extends from endocardium to pericardium, mural thrombi form, which may cause peripheral embolization, and a friction rub may be heard. Although the clinical picture is variable, severe pain is usually present and shock and heart failure are common. The electrocardiogram usually presents a characteristic, progressive pattern, consisting of RS-T elevation and deep Q waves followed by T-wave inversion as the RS-T segment returns to normal (Fig. 1). The electrocardiographic abnormalities are persistent and often permanent.

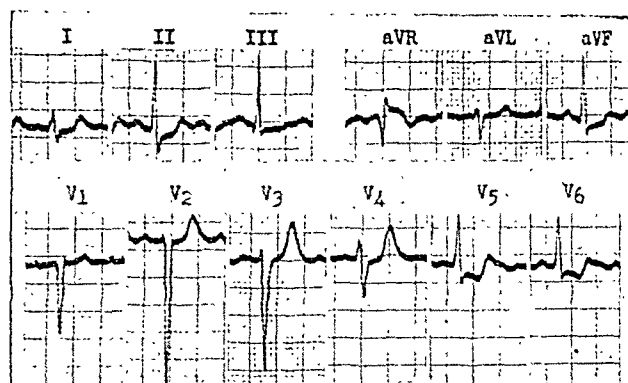


Fig. 1.—Electrocardiogram of a 38-year-old man with acute coronary insufficiency after effort, the standardized two-step exercise test. RS-T segments depressed in leads 1, 2, 3, and V₁, V₂, V₃.

ACUTE CORONARY INSUFFICIENCY

Acute coronary insufficiency includes several types of acute coronary episodes. The simplest is the classical brief attack of angina pectoris resulting from a temporary functional inadequacy of coronary circulation. It is usually precipitated by exertion, excitement, cold, or ingestion of food and is relieved promptly by glyceryl trinitrate and rest. These episodes usually last a few minutes, rarely more than half an hour. No matter how severe the pain, when the attack is ended the patient returns to his previous condition and is usually well.

We restrict the term acute coronary insufficiency to more severe attacks, in which pain is more prolonged or in which the process passes beyond the functional stage and results in necrosis or infarction of the myocardium. Consequently, shock, heart failure, a fall in blood pressure, fever, leukocytosis, and an increased sedimentation rate may appear, but they are usually less severe than in coronary occlusion. This is so because, unlike the massive, through-and-through infarct usually present in coronary occlusion, only focal disseminated areas of necrosis limited to the subendocardial region and papillary muscles ordinarily are produced by coronary insufficiency.

From the Cardiographic Department, Mount Sinai Hospital. Mrs. Beatrice Field assisted in collecting the data presented in this paper.

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Since the subpericardial layer is not involved, a pericardial rub is absent; also embolic phenomena do not occur, because the endocardium is spared. Because of the subendocardial localization of the ischemia or necrosis, in the electrocardiogram in coronary insufficiency there are RS-T depressions and T-wave inversions; RS-T elevation is absent, since the subpericardial layer is not involved, and there are no Q-waves because the infarct is not through and through (Fig. 2). The electrocardiographic alterations usually disappear within several days or weeks. One exception to these rules is coronary occlusion with true posterior infarction, which is not common. As it is ordinarily used, the term posterior infarction applies to infarction of the diaphragmatic surface. An infarct confined to the posterior surface produces an electrocardiographic pattern similar to that of coronary insufficiency. In addition, there is a large R-wave in lead V₁, but this is not diagnostic since it may be present normally.

Coronary insufficiency arises when there is a disproportion between the oxygen requirement of the myocardium and the supply immediately available.⁹⁸ For purposes of pathogenesis, cases of coronary insufficiency may be divided into two groups. In the first, the attack

cardial necrosis. These cases of coronary insufficiency are differentiated from those of coronary occlusion by the electrocardiographic pattern and the relatively rapid return of the electrocardiogram to its previous state.

MATERIAL

We have been investigating the mode of onset in coronary attacks for many years and in previous papers have reported our findings in 1,700 attacks of coronary

TABLE 1.—Types of Activity at Onset of 1,347 Attacks of Coronary Occlusion

Activity	No. of Attacks	%
Sleep	305	22.6
Rest	401	29.8
Ordinary mild activity.....	302	22.4
Moderate activity.....	117	8.7
Walking	198	14.6
Unusual or severe exertion.....	24	1.9
Total.....	1,347	100.0

occlusion.⁷ At present our studies cover 2,080 attacks and 100 episodes of coronary insufficiency. We obtained detailed histories of the activities of the patients during the eight weeks preceding the attack up to its actual onset. It is possible to determine a premonitory stage in almost half the cases of coronary occlusion.¹²

In Table 1 it will be seen that, in 1,347 attacks, the occlusion occurred during sleep in 22.6% of the cases, at rest in 29.8%, during usual, mild activity in 22.4%, during moderate activity in 8.7%, while walking in 14.6% and during unusual or severe exertion in only 1.9%. Mild activity included such routine functions as dressing, conversing or taking a shower at home, getting out of bed, sitting in a theater, attending a meeting, doing light housework, riding in a train or bus, and waiting in a doctor's office. Moderate activity consisted of work at a trade, such as painting, pressing, baking, or driving a car, bowel movement or enema, coitus, shopping, and climbing stairs. Unusual activity included sports, lifting or moving a load, and running.

The relation of coronary occlusion to effort was investigated from another point of view, i. e., occupation.

TABLE 2.—Occupations in 1,495 Cases of Coronary Occlusion

Occupation	No. of Patients	%
Workers and laborers.....	501	33.5
Store workers.....	89	6.0
White collar and office workers.....	138	9.5
Businessmen.....	180	12.0
Professional class.....	135	9.0
Housewives	295	20.0
None or retired.....	157	10.0
Total.....	1,495	100.0

Table 2 shows that all classes were encountered, including skilled and unskilled laborers, store and office workers, businessmen, and professional persons. As was to be expected, workers and laborers formed the largest group, 33.5%. The incidence of the other groups varied from 6% to 12%. It is noteworthy that 10% of the patients were retired. Table 3 discloses a close correlation between the groups in our series and the employed population of New York and New Jersey. In our series the incidence of workers and laborers was 6% less than

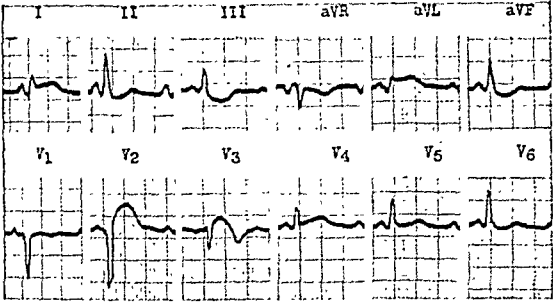


Fig. 2.—Electrocardiogram of a 53-year-old man three days after acute coronary occlusion. Q-wave in leads I, aVL, V₁, V₂, V₃, with RS-T segment elevations in I, aVL, and V₂, V₃, and V₄.

is precipitated by factors that increase the oxygen demands of the heart, decrease the coronary flow, or reduce the oxygen-carrying capacity of the blood. Thus, the attack may follow effort, excitement, trauma, sexual intercourse, straining at stool, extremes of heat or cold, tachycardia, shock, hemorrhage, heart failure, operation, anesthesia, hypoglycemia, various infections (including gastroenteritis), carbon monoxide poisoning, excessive smoking, chronic anemia, hyperthyroidism and hypothyroidism, hypertensive crises, Addison's disease, aortic stenosis, pulmonary embolism, and gallbladder and other abdominal diseases. In these cases, treatment of the etiological condition may be life-saving. For example, we have given up to 2,500 cc. of blood in acute hemorrhage, all within 24 or 36 hours.

In the second group of cases of coronary insufficiency, the episode is not related to any obvious event; it occurs spontaneously, as do practically all attacks of coronary occlusion.⁷ In these cases it may be assumed that changes are taking place in one or more coronary arteries, changes such as progressive narrowing or subintimal hemorrhage, which do not progress to occlusion but are sufficient to produce pain, on effort or at rest, and even subendo-

in the working population, the incidence of store and office workers and businessmen was 2% greater, and the incidence of professional persons was 4% greater. These differences are not significant. The slightly lower incidence of workers and laborers may be partly explained by the fact that laborers form a relatively small

TABLE 3.—Comparison of Occupations in Coronary Occlusion and General Population Groups

Occupation	Percentage	
	Patients with Coronary Occlusions	Labor Force, N. Y. Nov., 1946
Workers and laborers.....	48%	54%
Store, office, business.....	39%	37%
Professional workers.....	13%	9%
Total No. in All Occupations.....	1,013	3,280,824

proportion of the population of the hospital where our cases were studied. From our figures it may be concluded that occupation and social status do not affect the incidence of coronary occlusion. This opinion is shared by some authors,¹³ but the general belief, among physicians as well as lay persons, is that coronary occlusion much more frequently affects those whose work or occupation involves considerable mental activity, competition, anxiety, and stress, e. g., executives, business leaders, professional persons, foremen, and skilled workers.¹⁴ This is probably true of physicians, in whom coronary disease occurs more frequently than in the general population.¹⁵ It is notable, however, that their age at death is not greater.¹⁵

Tables 4 and 5 make it evident that the incidence of coronary occlusion varies little during the cold and warm seasons and during the day (7 a. m. to 7 p. m.) and night (7 p. m. to 7 a. m.). The incidence was only about 3% greater during the colder months and during the day, a difference which is not significant. Mintz and Katz⁸¹ also found no influence of season in coronary occlusion, but other authors believe that the disease is commoner in the cold weather.¹⁶

Among the 570 most recent acute coronary episodes collected by us, there were 370 attacks of coronary occlusion and 200 of coronary insufficiency, a ratio of almost 2:1. The actual incidence of acute coronary insufficiency is probably much higher, since, in several large series of sudden deaths of patients examined at necropsy, coronary insufficiency was found in 65% to 80% of the cases.¹⁷

TABLE 4.—Seasonal Incidence in 1,151 Attacks of Coronary Occlusion

Season	No. of Attacks	%
Winter.....	300	26.1
Spring.....	268	23.3
Summer.....	288	25.0
Autumn.....	295	25.6

Also, doubtless many cases of coronary insufficiency are too mild to cause the patient to consult a physician.

Table 6 shows the mode of onset in 100 attacks of coronary insufficiency. Fifty-six occurred at rest or during mild or moderate activity; the remaining 44 were associated with conditions decreasing the coronary flow, impairing the oxygen content of the blood, or increasing the work of the heart. The commonest factors were

hemorrhage, pulmonary embolism, effort, tachycardia, operation, excitement, and meals. Others included trauma, heart failure, acute cholecystitis and pancreatitis, gastroenteritis, hypertensive crises, carbon monoxide poisoning, asthma, and smoking. In all these cases the electrocardiogram presented RS-T depression and/or T-wave changes.

Our personal experience with trauma to the heart, other than penetrating wounds, is not extensive, but a study of the literature makes it evident that nonpenetrating injuries of the chest and abdomen, whether direct or indirect, can produce functional derangement of the heart (commotio cordis) or contusion.¹⁸ It is our belief that trauma rarely results in coronary occlusion, if at all; it occurs only if an artery is directly injured.¹⁹ The vast majority of conditions reported as traumatic coronary occlusion have actually been contusions of the heart,¹⁸ and the failure in the past to distinguish between these two conditions makes it imperative to re-evaluate the entire field of

TABLE 5.—Period of Day of Onset of 944 Attacks of Coronary Occlusion

Period of Day	No. of Attacks	%
7 A. M.—1 P. M.....	267	
1 P. M.—7 P. M.....	220	
7 A. M.—7 P. M.....	487	51.6
7 P. M.—1 A. M.....	218	
1 A. M.—7 A. M.....	239	
7 P. M.—7 A. M.....	457	48.4

TABLE 6.—Activity at Onset of 100 Attacks of Coronary Insufficiency

No unusual activity.....	56	Acute cholecystitis.....	1
Hemorrhage	10	Acute pancreatitis.....	1
Pulmonary embolism.....	8	Gastroenteritis	1
Unusual effort.....	6	Hypertensive crisis.....	1
Tachycardia	3	Postsympathectomy	1
Surgical procedure.....	3	Carbon monoxide.....	1
Excitement	2	Tobacco and alcohol.....	1
Meal	1	Addison crisis.....	1
Trauma	1	Asthma	
Acute left heart failure.....	1		

the effect of trauma on the heart.¹⁸ It will be necessary to differentiate contusion of the heart, coronary insufficiency secondary to trauma, and coronary occlusion. The electrocardiogram enables this distinction to be made in most cases, since RS-T elevation and Q waves appear, with rare exceptions, only in coronary occlusion.

COMMENT

When acute coronary occlusion and coronary insufficiency are differentiated, the latter is found to be a common condition.⁴ It is associated with a precipitating factor in one-third to one-half the cases. On the other hand, coronary occlusion follows unusual exertion in only 2%. It is because of these rare cases, in which coronary occlusion occurs immediately after strain and therefore seems to be directly related to it, that the relation of coronary occlusion to effort remains a moot question. If the incidence of attacks in our series occurring during sleep, rest, mild or moderate activity, and walking is compared with the percentage of time during the day usually spent in each category, a close correlation is found. Thus,

about half the attacks began during sleep and rest and the majority of persons spend half the day in this way. Therefore, these activities may be considered coincidental. Similarly, the association of only 2% of the coronary occlusion attacks with severe exertion is also coincidental. Most persons perform some unusual effort at least several times a day, e. g., lifting a load, moving furniture, running after a bus, or parking a car in a small space. If effort were a precipitating factor in coronary occlusion, the incidence of attacks during strain should be much greater.

Another reason for believing that coronary occlusion and effort are not causally related, even when they occur simultaneously, is the fact that the formation of a coronary thrombosis takes place over a variable period, which occasionally extends over several weeks.²⁰ During this interval premonitory symptoms are present in approximately half the patients, but there may be none at all. It is probable, therefore, that, in the rare cases in which the acute attack occurs during, or soon after, strain, the occlusion has already completely formed, but there were no symptoms of infarction, because of adequate collateral circulation, until the effort was performed. Therefore, the exertion may account for the appearance of symptoms and even death, but not for the coronary occlusion that had occurred spontaneously. This belief is supported by the observations of Yater and his associates, who found previously organizing thrombi in 38% of their cases of fatal coronary occlusion apparently associated with effort and in only 11% of those in which the patients died in bed.^{8m}

We believe coronary occlusion is the end result of the atherosclerotic process and in many cases is initiated by a subintimal hemorrhage. Some writers have assumed that effort, by suddenly raising aortic blood pressure, causes subintimal hemorrhage and, therefore, coronary occlusion; however, there is no evidence for this supposition, which is wholly theoretical. It has not been demonstrated that a rise in systemic pressure is transmitted to the coronary capillaries or that it may cause subintimal hemorrhage. Winternitz²¹ injected fluid into the coronary arteries post mortem at a pressure of 500 mm. without producing hemorrhage. Furthermore, at necropsy we found intimal hemorrhage as frequently in nonhypertensive hearts and in those of persons who had been bedridden as in hypertensive hearts and those of active persons. It is likely that subintimal hemorrhage is part and parcel of the arteriosclerotic process and is uninfluenced by external factors.

For similar reasons, we believe that bed rest does not induce coronary occlusion. It has been suggested that a drop in blood pressure and slowing of the circulation, which occur in shock or sleep, may be conducive to the formation of coronary thrombosis, but there is no proof of this contention.²²

The relation of coronary occlusion, coronary insufficiency, and angina pectoris to effort may be summarized as follows: Effort produces angina pectoris in almost 100% of cases and coronary insufficiency in about 50%; coronary occlusion occurs coincidentally with effort only in rare cases. This may be stated in another way. The majority of attacks of coronary occlusion occur during rest or sleep; coronary insufficiency often does; and angina pectoris rarely does.

It may be pertinent to point out that coronary occlusion almost never, if at all, results from the breaking off of sclerotic plaques in a diseased coronary artery, as has sometimes been suggested.²³

It is often asked whether one attack of coronary occlusion predisposes to a subsequent attack. In our opinion there is no such relationship. Occlusion occurs spontaneously in a diseased artery, and this process is not influenced by previous thrombosis and infarction in another area of the heart. The second attack often occurs when the patient is well and has made an excellent recovery from the first attack. It is the result of the underlying atherosclerotic process. Although in rare instances only one coronary artery is diseased when coronary occlusion has occurred, it may be assumed that, as a rule, other arteries are also sclerotic. A second occlusion may occur fortuitously in one of these at any time. Even when a subsequent attack occurs soon after the first, i. e., during the first six weeks, there is probably no causal relationship.

In industrial compensation the problem of determining the role of effort in the onset of coronary occlusion is complicated by economic considerations. In giving his history it is natural for the worker to be influenced by this factor. The vast majority of persons are instinctively honest, but the need for economic compensation may distort their judgment and point of view. It is our opinion that only once in 10 to 20 cases is a true story obtained. Frequently a worker who has experienced angina for a number of years and has consulted physicians for the condition has denied ever having been sick.²⁴ Also, we remember the butcher's helper who sustained a coronary occlusion on a Sunday during a card game at a friend's house but wished to report that the attack had occurred on Thursday during work. It is not uncommon for the laborer, on admission to the hospital, to state that the attack occurred spontaneously; yet several weeks later he changes his story and relates the onset of the attack to some strain. He is also likely to record as very unusual and strenuous activity which for him has been routine for many years. Obviously such work, even if severe, should not be blamed for producing coronary occlusion. Even when there is no conscious falsification, most persons tend to relate the onset of pain to a specific event, even if there is no actual connection. Furthermore, they are inclined to overlook or forget the fact that they had not felt well prior to the unusual effort. In the near future it is likely that the compensation laws will be amended so that the worker will receive compensation whenever he becomes ill while at work, regardless of previous illness. This has already been done in New York State. It will then be possible to obtain more accurate histories and, thus, a truer idea of the relation between effort and coronary occlusion. We have already alluded to the fact that the process of formation of a coronary occlusion usually goes on for some time. During this period symptoms may or may not be present. In many cases in which coronary occlusion is supposed to have been precipitated by effort, a detailed history discloses the onset of symptoms prior to the exertion. We believe that, in bona fide cases of coronary occlusion which start during or immediately following strain, the occlusion has already formed, perhaps asymptotically. The strain was sufficient to produce

symptoms of infarction and even death. The effort may be compensable as an aggravating factor but not as a causative one.

It is obvious that, in the evaluation of compensability, numerous complicated elements of the case must be considered and complete neutrality practiced by both the worker and the carrier. Each case must be decided on the basis of a complete history, in which the following points are considered: (1) evidence of previous cardiac symptoms or disease; (2) exact time of onset of symptoms in relation to the strain; (3) the type and severity of the strain; and (4) the type of disturbance sustained, i. e., coronary thrombosis or insufficiency.

Not infrequently, in compensation cases involving the occurrence of coronary occlusion after effort, the patient claims that he was completely asymptomatic prior to the strain and that, therefore, the effort caused the disease. Such a history, even if true, does not establish causal relationship, since it may be taken for granted that coronary artery disease always antedates coronary occlusion, whether or not there were symptoms prior to the occlusion.

The interval elapsing between an effort or trauma and the onset of coronary episodes is of great importance in determining causal relationship. In coronary insufficiency, symptoms usually set in immediately; if they appear after one to two hours, it is unlikely that they were caused by the strain. In coronary occlusion, the sequence is less direct since it may take some time for a thrombus to form. However, one would expect some symptoms, such as pain or weakness, within the first day or two if there has been a change in an artery. If there are no symptoms for 48 hours following effort or trauma, and a coronary occlusion develops later, it was probably not caused by the effort or trauma.

One is always faced with the question of length of disability following recovery from a coronary occlusion. Obviously, this varies in each case. Disability may be permanent, for example, if congestive failure sets in. However, many persons, particularly those under 50, recover completely and are able to return to work within three to six months.²⁵ About half the patients are able to resume moderate work and are in a better psychological state when they do. How strenuous the work may be must be determined in each case. It is a great error, in many cases, to restrict activity more than is essential. If working induces angina which is not present at rest, restriction is indicated. In general, it is wise to avoid a job in which collapse will endanger the safety of others. In selected cases who have been observed for a considerable time, manual labor of moderate degree may be allowed under supervision.²⁴

Since acute coronary insufficiency depends on an inadequate coronary flow, which may be initiated by numerous conditions, it may be compensable. This is true, for example, when it follows effort, trauma, or operation. As a rule the period of disability does not exceed several weeks, but coronary insufficiency may be fatal and occasionally leads to incapacitating symptoms, such as angina, for a varying period. It may even lead to congestive failure for a considerable period or even for life. If, as is usual, the symptoms are brief and the electrocardio-

gram returns to normal within a week or two, the period of compensation may be one or two months.

A difficult question is posed by the patient who had never experienced angina prior to a specific unusual strain and then complains of a persistent anginal syndrome. The symptoms immediately following the effort may be ascribed to acute coronary insufficiency and may, therefore, continue for one to several weeks or possibly several months; during this period compensation is warranted. However, this should not lead to chronic angina unless we invoke the theory of setting off a trigger mechanism. In that case it is reasonable to assume that the anginal syndrome probably would have appeared spontaneously at about the same time or as the result of some other trigger mechanism. The problem becomes even more complex if, following the strain and the subsequent angina, coronary occlusion occurs after several months. It is probable that there is no causal relationship between the effort and the occlusion in these circumstances.

The answers to some of these questions cannot be given with certainty, and much work remains to be done in this field. It is essential to approach the problem in a spirit of impartiality and to pay particular care to the use of correct terminology. In this way alone will it be possible to clarify much of the confusion and disagreement that now exist.

SUMMARY

The activities preceding the onset have been studied in 2,080 attacks of acute coronary occlusion and in 100 episodes of acute coronary insufficiency.

Coronary occlusion and insufficiency can be differentiated electrocardiographically in 95% of the cases. Coronary occlusion produces through-and-through infarction. Coronary insufficiency causes only subendocardial necrosis. Coronary insufficiency is at least as common as coronary occlusion.

The onset of coronary occlusion was associated with unusual effort in only 2% of the cases. Reasons are given for considering the association coincidental. Coronary occlusion is a spontaneous event in the course of atherosclerosis. Occupation, season, and time of day did not influence the incidence of coronary occlusion. The onset was spontaneous in 56 of 100 attacks of coronary insufficiency. In the remaining 44 the commonest precipitating factors were hemorrhage, pulmonary embolism, effort, tachycardia, operation, excitement, and meals. Angina pectoris almost always is related to effort; coronary insufficiency is related to effort in about half the cases and coronary occlusion only rarely and coincidentally. Trauma may produce contusion of the heart or coronary insufficiency. The criteria for establishing compensability in acute coronary episodes are discussed. The following theoretical problems are considered: relationship of one attack of coronary occlusion to a subsequent one; length of disability and employability following coronary occlusion; and causal relationship of effort to permanent angina pectoris. In general, the outlook for the worker after coronary occlusion is much better than was formerly thought. One-half to two-thirds of patients return to gainful employment within one year. In coronary insufficiency the prognosis is even better.

Fifth Ave. and 100th St.

RADICAL PROSTATECTOMY AFTER PREVIOUS PROSTATIC SURGERY

TECHNICAL PROBLEMS ENCOUNTERED IN TREATMENT OF OCCULT PROSTATIC CARCINOMA

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It has been demonstrated that Young's radical perineal prostatectomy, which involves removal of the prostate and the seminal vesicles, is the treatment of choice for early cancer of the prostate gland.¹ Occult or unsuspected carcinoma of the prostate discovered accidentally after biopsy or conservative prostatectomy by any route is usually early. It probably occurs in at least 9% to 10% of men over 50 years of age² and is thus a real problem.

Hinman and Hinman, in discussing the justification for radical prostatectomy after previous operative discovery of unsuspected prostatic carcinoma, concluded, "... radical perineal prostatectomy seems indicated if an apparently localized area of carcinoma is found either on transurethral resection or on open prostatectomy."³ Nesbit and Baum have recently questioned the above statement in the light of present available survival statistics with conservative therapy.⁴

The present study concerns 23 cases of radical prostatectomy after previous prostatic surgery from August, 1948, to March, 1951. Since during this same period a total of 69 patients were subjected to radical prostatectomy in the Brady Urological Institute, Johns Hopkins Hospital, the present series represents about a third of all the radical operations on the prostate performed there in the period of study. This figure emphasizes the importance of evaluation of these cases. Because of the brief period since operation, no attempt is made in this paper to justify radical prostatectomy for occult carcinoma in terms of curability. Jewett's study¹⁰ has provided ample grounds for expecting over 50% five-year cures in cases with early carcinoma treated by radical prostatectomy.

This series of 23 patients subjected to radical prostatectomy after previous operation on the prostate was collected in a period of less than three years and attests to the enthusiasm in this clinic for radical prostatectomy in "selected cases" when the surgeon believes the cancer is curable. Current opinion and practice at the Brady Urological Institute may be expressed as follows: "When carcinoma of the prostate is demonstrated in a patient with a life expectancy of 10 years or more, it should always be removed by radical prostatectomy when the surgeon believes it is totally removable and when the patient is a good operative risk."

This paper is an attempt to answer or discuss the following questions: Does radical prostatectomy after previous prostatic surgery differ technically from the operation in an untouched case? Should technical problems influence the operator's judgment? What is the optimum time between operations? What is the operative route of choice? Are complications greater? Are operative mortality and morbidity significantly influenced in these cases?

Interest in these questions was aroused when a 57-year-old Negro (Case 1, Table 3) came under my care. On Sept. 1, 1948, uncomplicated suprapubic prostatectomy was performed. The pathologist's report de-

scribed hyperplasia and previously unsuspected adenocarcinoma of the prostate. Twelve days later radical perineal prostatectomy was undertaken but had to be abandoned in favor of subtotal perineal prostatectomy because of operative difficulties. The usual perineal exposure was uncomplicated, but radical prostatectomy was impossible because the remaining prostate was so thin and the tissues were so friable and edematous from the previous procedure that the prostate was removable only piecemeal. A comment at the end of the operative note states, "This was the operator's first attempt to remove radically a carcinoma of the prostate following prostatectomy by another method. I believe the lesson to be learned is that, if this procedure is to be carried out, it should be done at a greater interval after the previous operation."

TABLE 1.—Evaluation of Operative Difficulty

Degree of Difficulty	Interpretation
0	No unusual difficulty
1	Operator notes altered conditions
2	Adhesions and/or obliteration of landmarks
3	Prostate removed piecemeal, or serious operative complication
4	Operation abandoned or unsatisfactory to surgeon

After the preceding experience, it was of interest to observe similar cases. The 23 radical operations discussed here were done by eight different surgeons. Four of them were my own cases. I assisted the operator in eight cases and observed five others. The other six are evaluated from the operative notes or from conversation with the surgeon. An estimate of degree of operative difficulty was made in each case (Table 1) and represents, of course, my subjective judgment of the situation. No difficulty or first degree difficulty was interpreted as indicating that the previous operation did not materially affect the later radical operation. Third and fourth degree difficulties marked serious interference with the normal course of the operation and suggested that the operation could probably not be expected to effect a cure.

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3. Hinman, F., Jr.: Personal communication to the author.

4. Nesbit, R. E. C.: Personal communication to the author.

4). The end result in this case, however, is satisfactory as it is in most of the others.

Inspection of the last column in the tables shows the varying degrees of difficulty experienced in radical prostatectomy following different types of operations. In general, but not always, the operations after previous prostatic adenomectomy by any of the open routes have been very difficult. Thus in five of the seven cases in Tables 2 and 3 there was serious interference with the normal operative procedure. By contrast, radical prostatectomy after previous transurethral resection was usually un-

and led to the complication of severance of the ureter and piecemeal removal of the carcinomatous prostate. The end result in this case is to date excellent, in spite of the severe operative trauma, but in this and some of the other extremely difficult cases one wonders whether the operation was justified.

An attempt was made to learn of the experiences in other clinics under similar circumstances. Some surgeons could not recall having done a radical prostatectomy after previous prostatic surgery. Others remembered a few cases after transurethral operations, where the oper-

TABLE 4.—*Radical Prostatectomy After Perineal Biopsy*

Case No.	Date of Operation	Time Between Biopsy and Radical Prostatectomy	Type of Radical Prostatectomy	Pathology Specimen	Post-operative Hospitalization, Days	Post-operative Incontinence	Complications	Late Post-operative or Present Status	Estimated Operative Difficulty *
1	April, 1919	2 days	Perineal	Carcinoma of prostate	23	0	Transient ulnar palsy	Excellent	2
2	Aug., 1950	7 days	Perineal	Carcinoma of prostate	21	Slight stress	None	Satisfactory	0
3	Aug., 1950	6 weeks (Previous TUR's † 10 yr.; 5 wk.)	Perineal	Carcinoma of prostate	17	0	Left ureter cut at operation; repaired	Excellent	Probably easier 3
4	Feb., 1951	7 days	Perineal	Carcinoma of prostate	23	0	None	Excellent	1
5	Feb., 1950	6 hr.	Perineal	No pathology report	27	0	Pneumonia, hemorrhoids, slow healing	Good	0
6	Jan., 1951	5 days	Perineal	Carcinoma of prostate	40	0	Thrombophlebitis	Good	0
7	Jan., 1951	5 days	Perineal	Carcinoma of prostate	19	Stress incontinence, early	None	Good	Easier 3

* See Table 1. † Transurethral resection.

TABLE 5.—*Radical Prostatectomy After Transurethral Resection*

Case No.	Date of Operation	Time Between TUR* and Radical Prostatectomy	Type of Radical Prostatectomy	Pathology Specimen	Post-operative Hospitalization, Days	Post-operative Incontinence	Complications	Late Post-operative or Present Status	Estimated Operative Difficulty †
1	Aug., 1918	4 mo.	Perineal	Carcinoma of prostate	35	0	Stricture; dilatation elsewhere	Excellent	3
2	Sept., 1918	4 yr.	Perineal (rad. sem. tract)	Seminal tract tuberculosis	19	0	None	Excellent	0
3	March, 1919	2½ mo. 4 wk.	Radical cystect., perineal & abdom.	Carcinoma of prostate	30	0	None	Excellent	2
4	April, 1919	2½ mo.	Perineal	Carcinoma of prostate	28	Slight stress	None	Satisfactory	0
5	May, 1919	3 wk.	Perineal	Carcinoma of prostate	37	Incontinent	Wears urethral clamp	Unknown	1
6	Oct., 1919	11 mo. 2½ mo.	Retro-pubic	Carcinoma of prostate	14	0	Urethral stricture; cystostomy	Unknown	1
7	Sept., 1950	1 mo.	Perineal	Carcinoma of prostate	18	0	None	Satisfactory	1
8	Jan., 1951	10 days	Perineal	No carcinoma	18	0	Stricture	Satisfactory	0
9	Dec., 1950	10 days 5 days	Perineal	No carcinoma	21	0	None	Excellent	0

* Transurethral resection. † See Table 1.

complicated or presented minimal difficulties. The operators often noted the area of resection and sometimes found the prostatic capsule rather thin, but only in one of the nine cases in Table 5 was operation inordinately difficult. The same was true of operations performed after perineal biopsy, particularly when they were performed soon after, before complete healing in the operative site. One patient (Case 3, Table 4) was an exception to this; he had had two previous transurethral operations and a perineal biopsy before the radical operation. In this case all landmarks were obliterated by adhesions, which necessitated sharp dissection throughout the operation

and led to the complication of severance of the ureter and piecemeal removal of the carcinomatous prostate. The end result in this case is to date excellent, in spite of the severe operative trauma, but in this and some of the other extremely difficult cases one wonders whether the operation was justified.

active difficulty was not increased. Smith⁵ recalled a total perineal prostatectomy that he did two weeks after a previous perineal enucleation. His operative note describes "some difficulty until the lateral margins of the prostate were identified after which the operation was carried out in the usual manner." Shaw⁶ states that radical prostatectomy in three or four cases after perineal biopsy at a previous operation was "not found to be technically difficult." These results are similar to those in Table 4 of

5. Smith, G. G.: Personal communication to the author.

6. Shaw, E. C.: Personal communication to the author.

this series. Hinman⁷ reviewed operative notes in nine of the cases he had previously reported.^{1†} One of the patients, operated on in 1942, had had suprapubic prostatectomy in 1937 and two transurethral resections in 1938. The operative note describes "... great difficulty, because of fibrosis incident to previous operative procedures. . . ." This closely parallels some of the cases summarized in Table 3. The other cases in his series after transurethral resection were often more difficult than an untouched case, but the difficulties did not prevent radical prostatectomy. In summary, the operative difficulties in his clinic were comparable to those observed here.

RADICAL PROSTATECTOMY AFTER TRANS- URETHRAL RESECTION

Prostatic carcinoma was demonstrated in the specimen removed at radical prostatectomy in six of eight cases after previous transurethral resection had shown cancer (Table 5). This seems to indicate that resection alone in this group did not offer hope of total removal and possible cure in any substantial number of cases. Since previous resection, except in one case, did not markedly increase the difficulty of later total prostatectomy, it would seem that radical prostatectomy is justified in this group if the operator feels the disease is curable. The time interval between first and second operation did not seem to matter, though multiple previous operations in this group (as in Hinman's series⁷) usually tended to increase the operative difficulty.

RADICAL PROSTATECTOMY AFTER PERINEAL BIOPSY

It is the custom in this clinic to perform perineal biopsy for frozen section study of suspected malignant lesions of the prostate which are considered curable. In the great majority of cases radical perineal prostatectomy follows immediately on the positive report of carcinoma from frozen section. Occasionally, when the frozen section is reported negative and the patient is returned to bed without further operation, a subsequent report on the permanent sections from the biopsy specimen shows carcinoma. These cases make up Table 4. In all cases of this group in which a pathologist's report was rendered on the specimen after radical prostatectomy, carcinoma was demonstrated. Operative difficulty, except in Cases 3 and 7, was not materially increased, and the radical operation seems well justified in these cases when cure is possible. The time interval here is probably important, as the surgeons usually approached the prostate through the same incision previously employed, before healing was complete. In some cases this actually made the operation easier. It would seem from study of this group that the radical operation should be done two to seven days after perineal biopsy if possible.

RADICAL PROSTATECTOMY AFTER OPEN ADENO- MECTOMY BY ALL METHODS

As mentioned before, the greatest operative difficulties were encountered after previous open enucleation of the prostate by any route. Even when the same route was used, these difficulties occurred not so much in the approach as in the attempted complete surgical removal of the remaining prostate and vesicles. In only two of the

seven cases in Tables 2 and 3 was the operation without severe technical difficulty. In two of the cases operation was abandoned as "impossible." Also of interest in the cases after open adenomectomy was the fact that no carcinoma was reported by the pathologists in three of the six cases in which an operative specimen was submitted. This suggests that the "occult carcinoma" found in the previously enucleated adenoma was totally removed by the first operation in half the cases, though admittedly the series is too small to be significant in this report. Still, in some of the remaining cases in which carcinoma was demonstrated, it may not have been completely removed by the radical operation. In Case 2, Table 2, the operative note describes removal of the left seminal vesicle and vas separately, and a follow-up note two years later describes a nodule in that area that may represent local recurrence, though the patient is in excellent condition and completely asymptomatic. In Case 1, Table 3, carcinoma was definitely left behind as it was in Case 4, Table 2, where no attempt was made to remove it. The time interval between first and second operation may be important here. In the cases in which operation was done at 9 and 12 days, and in 1 of the cases at 18 days, friable tissue, edema, and marked inflammation were noted in the prostate, making the conventional easy complete removal of an intact specimen impossible. It is not proved from this study, but it seems likely that radical prostatectomy after previous open enucleation should be postponed for at least 30 days if it is to be done at all.

The question of the optimum route of removal is not settled here. In this clinic the perineal approach is favored as being easy and safe, allowing for complete exposure and removal of the whole specimen under direct vision. It also allows good anatomical closure under vision. Radical retropubic prostatectomy, particularly after a previous perineal approach, may have its useful place. This may be particularly true after many months have elapsed between the first and second operation and firm scarring has occurred. It would appear, however, from the data in Tables 2 and 3 that the approach to the prostate via the retropubic method (after previous perineal surgery) or via the perineal method (after previous suprapubic or retropubic operation) is of no particular advantage or disadvantage. The operator should probably use the approach for which he is best trained.

SUMMARY AND CONCLUSIONS

Unexpected discovery of carcinoma in prostatic tissue removed by previous operation raises the question of whether radical prostatectomy should be performed in such cases. This study does not answer the question directly but attempts to aid in making the decision. An opinion is expressed: When carcinoma of the prostate is demonstrated in a patient with a life expectancy of 10 years or more, it should always be removed by radical prostatectomy when the surgeon believes it is totally removable and when the patient is a good operative risk. The question of removability and technical problems encountered in radical prostatectomy after previous prostatic surgery are discussed in relation to a series of questions which are answered here:

Radical prostatectomy after previous prostatic surgery often differs technically from the operation in an untouched case. It may be more difficult. After transure-

7. Hinman, F., Jr.: Personal communication to the author.

thral resection or perineal biopsy, the difficulties are slight or nonexistent. After open adenomectomy by any route, radical prostatectomy is nearly always more difficult and may be impossible.

Technical problems should influence the operator's judgment and decision concerning operability; i. e., in some cases there is no use to attempt radical prostatectomy if it is foredoomed to failure (Case 1, Table 3; Case 2, Table 2). In general, the consideration of technical difficulties need not enter into the question of operation after previous transurethral resection or perineal biopsy. After previous open adenomectomy, they should be carefully weighed in the decision to operate or not to operate.

The optimum time between the first operation, when unexpected operable carcinoma is discovered, and subsequent radical prostatectomy depends on the type of previous operation. In cases in which radical prostatectomy is to follow transurethral resection or perineal biopsy, the sooner the better. After previous open operations, an interval of at least a month is probably advisable.

The operative route of choice depends on the surgeon's training. Radical perineal prostatectomy is favored in this clinic on the basis of exposure and visibility both for removal and for closure. There may be some advantage after previous operation by one route to do the radical by another, though this is not demonstrated in this small

series. The surgeon should choose the route for which he is best trained.

Complications may be greater when radical prostatectomy is done after a previous operation on the prostate, particularly after previous open operation. The difference is slight, however, except for operative difficulties, and this factor should not necessarily influence the surgeon's decision regarding the advisability of operation.

Operative mortality and morbidity are not significantly influenced in these cases.

It is concluded:

1. Radical prostatectomy after open adenomectomy by any route is almost always more difficult and is sometimes impossible. When the operation is undertaken, it probably is wise to wait at least one month or longer until complete healing has occurred.

2. Radical prostatectomy after previous perineal biopsy is usually as easy or easier than in an untouched case, provided the operation is done soon after biopsy. It should always be undertaken when a cure is possible.

3. Radical prostatectomy after previous transurethral resection showing unexpected carcinoma of the prostate is little or no different from a case without previous operation. Radical prostatectomy should always be done as soon as possible under these circumstances if the operator thinks that the cancer is curable and the patient is a good surgical risk with a life expectancy of 10 years or more.

VAGOTOMY IN THE TREATMENT OF GASTROJEJUNAL ULCERATION

A POSTOPERATIVE CLINICAL AND LABORATORY STUDY

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and

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The clinical features and the immediate postoperative results have been studied in 118 cases of gastrojejunal ulcer and four cases of gastroduodenal ulcer (table 1) in which vagotomy has been performed at the Mayo Clinic from 1945 to January, 1951. In the group in which the abdominal approach was used, marked jejunitis or actual ulcer with crater found at operation is included as a case of gastrojejunal ulcer. In cases in which the thoracic approach was used, the diagnosis was based on the clinical and laboratory findings. Results have been determined one to five years after operation by reexamination and laboratory studies in 13 of these cases and from questionnaires in 84. During the interval under consideration more patients returned for examination and laboratory studies, but these figures represent the means by which the latest information was obtained. Seventeen patients were operated on less than one year before the date of this writing.¹ No follow-up data were available on four patients.

Besides the 122 cases of gastrojejunal ulceration, we have studied eight cases of gastrojejuno-colic fistula in which vagotomy was performed. Follow-up studies of more than one year were available in seven of these cases.

There were two hospital deaths in the series; one was due to cerebral hemorrhage one month after operation and the other to uremia on the 26th postoperative day. Two other patients died of unrelated conditions 6 weeks and 13 months, respectively, after vagotomy (table 1).

The symptoms and signs of gastrojejunal ulceration are recurrent intractable pain, hemorrhage that has proved refractory to medical management, roentgenologic evidence of a gastrojejunal ulcer, a nonfunctioning gastroenteric stoma, or reactivation of a duodenal ulcer, which when it occurs is always secondary to a malfunctioning gastroenteric stoma. These are considered indications for operations.

PERTINENT OBSERVATIONS

In 47 of our cases gastrojejunal ulcer developed after gastroenterostomy. The gastroenterostomy was performed an average of 9.3 years prior to the vagotomy

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1. We believe that this is too short a period in which to evaluate results.

(table 2). In the 75 cases in which gastrojejunal or gastroduodenal ulcer developed after gastric resection, the average lapse of time between gastric resection and vagotomy because of symptoms of recurring ulceration was 3.3 years.

In 34 of the cases of gastrojejunal ulcer after gastroenterostomy the abdominal approach was used. Thirty of these patients had had previously performed posterior gastroenterostomy, and four had had anterior anastomosis.

The abdominal approach was used for vagotomy in 31 cases of gastrojejunal ulcer after gastric resection. In 12 cases less than 70% of the stomach had been resected previously. In two of the four cases of gastroduodenal ulceration, the ulcer developed after less than 70% of the stomach had been resected and Billroth I anastomosis performed. Four of the gastrojejunalocolic fistulas occurred after posterior gastroenterostomy, three after gastric resection with posterior colic anastomosis, and one after gastric resection with antecolic anastomosis.

66% accurate in demonstrating gastrojejunal and gastroduodenal ulceration. This is in contrast to 97% accuracy in demonstration of duodenal ulceration. In our series, figures, of course, can be presented only from the 68 cases of gastrojejunal or gastroduodenal ulcer in which the transabdominal type of vagotomy was used, since only by this method could the presence of a gastrojejunal or gastroduodenal ulcer be verified. Of these 68 patients, 13 were found at operation to have marked jejunitis with no definite evidence of an ulcer crater. The roentgenologic diagnosis of jejunitis was made in 2 of these 13 cases preoperatively, and no abnormality was apparent in the roentgenograms in the other 11 cases. In 37 (67.2%) of the remaining 55 cases in which gastrojejunal or gastroduodenal ulceration was proved surgically, a correct preoperative roentgenologic diagnosis was made. In one case a roentgenologic diagnosis of large gastrojejunal ulcer was made and only jejunitis was found at operation. These findings illustrate the value of the abdominal approach in order to verify the

TABLE 1.—Cases of Gastrojejunal and Gastroduodenal Ulcer

Type of Operation	No. Patients	Approach		Follow-Up												No Follow-Up	Deaths
				1 Yr.		2 Yr.		3 Yr.		4 Yr.		5 Yr.		Less Than 1 Yr. P.O.			
		E *	Q †	E	Q	E	Q	E	Q	E	Q	E	Q				
Gastrojejunal ulcer after gastroenterostomy																	
Vagotomy alone	39	13	26	2	8	1	10	..	4	1	7	..	1	4	..	1	
Vagotomy and gastric resection.....	3	..	3	..	2	..	..	..	..	..	..	..	..	1	..	..	
Vagotomy and anastomosis taken down.....	5	..	5	..	1	..	..	..	..	1	1	..	2	..	..	..	
Gastrojejunal ulcer after gastric resection																	
Vagotomy alone	62	40	22	..	7	3	11	..	14	3	7	..	3	8	4	2	
Vagotomy and re-resection.....	9	..	9	2	..	..	3	..	..	..	..	..	..	3	..	1	
Gastroduodenal ulcer after gastric resection																	
Vagotomy alone	2	1	1	..	..	..	..	..	..	1	..	..	..	1	..	..	
Vagotomy and re-resection.....	2	..	2	..	..	..	2	..	..	..	..	..	..	..	..	..	
Total	122	54	68	4	18	4	26	0	18	5	16	0	6	17	4	4	

* Examination. † Questionnaire.

Hemorrhage.—Of the 41 patients (table 3) followed one to five years after vagotomy for gastrojejunal ulcer developing after gastroenterostomy, 16 had had moderate hemorrhage and seven massive hemorrhage before vagotomy. After vagotomy two of these 41 patients had moderate hemorrhage. In 22 of 56 patients who had gastrojejunal ulcer after gastric resection, traced one to five years, hemorrhage was moderate and in nine it was severe. After vagotomy moderate hemorrhage had occurred in two of these cases and severe hemorrhage occurred in one. All three patients had hemorrhages after vagotomy alone. None of the four patients who had gastroduodenal ulcer after Billroth I resection hemorrhaged either before or after vagotomy.

Accuracy of Roentgenograms in Demonstration of Gastrojejunal Ulcer.—Because of the position and often rapid emptying of the stomach through the gastroenteric stoma, roentgenologists at the clinic² claim to be only

diagnosis whenever a study of the effects of vagotomy is being made.

PHYSIOLOGIC STUDIES

Acidity.³—Studies reported herein were carried out on patients who were examined for gastric acidity one to five years after vagotomy. Gastric acidity was reduced below preoperative levels in six of the seven cases in which vagotomy alone had been performed for gastrojejunal ulcer after gastroenterostomy and in all 12 such cases in which it had been performed for gastrojejunal ulceration after gastric resection. It is appreciated that such studies may be suspected of error owing to reflex of alkaline duodenal contents and biliary and pancreatic secretion into the stomach.

Motility.—Vagotomy alone reduced gastric motility immediately in 54.6% of 11 cases of gastrojejunal ulcer after gastroenterostomy and in 42.1% of 19 cases of gastrojejunal ulcer after gastric resection in which motility was studied. One to five years after vagotomy alone, however, motility was found to be reduced or absent on reexamination in 16.7% of 12 cases of gastrojejunal ulcer after gastroenterostomy and in 8.3% of 12 cases of gastrojejunal ulcer after gastric resection. Observations have been made in too few cases after other operations to be significant.

2. Kirklin, B. R.: Roentgenologic Determination of Normal and Abnormal Results Following Operation on the Stomach and Duodenum, *Am. J. Roentgenol.* 33: 468 (April) 1935; Personal communication to the authors.
3. Walters, W., and Belding, H. H., III: A Postoperative Physiologic and Clinical Study of Gastric Vagotomy in 130 Cases, *South. M. J.* 44: 326 (April) 1951; Physiologic and Clinical Studies of Vagotomized Patients; a Study of 331 Patients, *A. M. A. Arch. Surg.* 62: 183 (Feb.) 1951. Walters, W., and Belding, H. H., III: Physiological Effects of Vagotomy; a Study of 331 Patients, *J. A. M. A.* 145: 607 (March 3) 1951.

Insulin Tests.—Our method of performing the insulin test and criteria for a satisfactory test and negative or positive results differ somewhat from those of other investigators⁴ and have been described in detail in previous publications. We have found a 75% good correlation⁵ between results of the test and clinical results in

TABLE 2.—Time Between Gastric Resection or Gastroenterostomy and Subsequent Vagotomy

Lesion	Cases	Months		Years				
		Less Than 6	6-12	1-2	2-5	5-10	10 or More	
Gastrojejunal ulcer after gastroenterostomy	47	1 2.1%	2 4.2%	2 4.2%	9 19.2%	13 27.7%	20 42.6%	
Gastrojejunal or gastroduodenal ulcer after gastric resection.....	75	8 10.7%	10 13.3%	22 29.3%	22 29.3%	8 10.7%	5 6.7%	

our entire group of cases. However, of the six patients in the entire group who had proved recurrences five had undergone insulin tests, and for four of them results were negative.

CLASSIFICATION OF RESULTS

We have classified results as stated in previous papers in three categories: (1) excellent when the patient had no symptoms of ulcer and no evidence of disturbances of motility secondary to the vagotomy, such as gastric retention, diarrhea, or bloating; (2) unsatisfactory when symptoms of disturbances of motility are present or when a return of pain would lead one to suspect the return of a recurrent ulceration but such recurrent ulceration is not proved; and (3) poor when recurrent ulceration is proved by roentgenologic examination, at operation, or both. Results were determined one to five years after vagotomy in 94 cases of gastrojejunal ulceration and in three additional cases of gastroduodenal ulcer.

RESULTS IN CASES OF GASTROJEJUNAL ULCER AFTER GASTROENTEROSTOMY

Vagotomy Alone.—In 11 of the 34 cases (table 4) vagotomy alone was performed by the transthoracic approach with excellent results in five, unsatisfactory

TABLE 3.—Follow-Up Studies on Fifty-Four Patients Who Hemorrhaged Before Vagotomy for Gastrojejunal Ulcer

Operation Preceding Ulcer	Corrective Procedure	Moderate		Massive	
		Before Vagotomy	1 to 5 Yr. After Vagotomy	Before Vagotomy	1 to 5 Yr. After Vagotomy
Gastroenterostomy	Vagotomy alone	14	1	6	0
	With gastric resection	1	0	0	0
	With anastomosis taken down	1	1	1	0
Gastric resection	Vagotomy alone	20	2	7	1
	With gastric resection	2	0	2	0
Total cases		38	4	16	1

results in five, and a poor result in one. The last patient had recurrence of the pain of ulcer three months after vagotomy, and six months after vagotomy the roentgenogram showed evidence of recurrent gastrojejunal ulceration. The diagnosis was confirmed at subsequent gastric resection. The insulin test in this patient gave a negative result. In 23 of these 34 cases the abdominal

approach was used; the results were excellent in 16 and unsatisfactory in seven, in two of which there were symptoms of recurring ulceration.

Three of the patients in the entire group who had unsatisfactory results reported recurrent ulcer pain 1 year, 18 months, and 2½ years, respectively, after vagotomy alone. One of these three also reported a moderate gastrointestinal hemorrhage one year after vagotomy. In all three of these cases recurrence of ulcer was suspected, but the recurrence, of course, was not proved, and thus the results were classified as unsatisfactory. The results by years after vagotomy and by type of approach are shown in table 4.

Vagotomy Plus Excision of Gastrojejunal Ulcer and Closure of Openings in Stomach and Jejunum.—Follow-up data were available on all five patients one to five

TABLE 4.—Results of Vagotomy in Cases of Gastrojejunal Ulcer After Gastroenterostomy

Operation	Approach	Year	No.	Results			Symptoms of Ulcer	
				Excel- lent	Un- sat- is- fac- tory	Poor	No	Yes
Vagotomy alone	Thoracic	1	2	1	..	1	..	..
		2	3	2	1	..	..	..
		3	2	1	1	..	..	..
		4	3	..	3	..	..	..
		5	1	1	..	..	..	..
		Total	11	5 45.4%	5 45.4%	1 9.2%	9 81.8%	2 18.2%
	Abdominal	1	8	6	2	..	..	..
		2	8	6	2	..	..	..
		3	2	1	1	..	..	..
		4	5	3	2	..	..	..
		5	..	..	..	..	..	..
		Total	23	16 69.6%	7 30.4%	..	21 91.3%	2 8.7%
Vagotomy and gastric resection	Abdominal	1	2	1	1	..	..	..
		2	..	..	..	..	..	..
		3	..	..	..	..	..	..
		4	..	..	..	..	..	..
		5	..	..	..	..	..	..
	Total	2	1 50%	1 50%	..	2 100%	..	
Vagotomy and anas- tomosis taken down	Abdominal	1	1	..	1	..	..	..
		2	..	..	..	..	..	..
		3	..	..	..	..	..	..
		4	2	1	..	1	..	..
		5	2	2	..	..	..	..
	Total	5	3 60%	2 20%	1 20%	3 60%	2 40%	
Grand total			41	25	14	2	35	6

years after vagotomy. Three had obtained excellent results, one an unsatisfactory result due to recurrent ulcer type of pain one year after vagotomy, and one a poor result. This last patient showed recurrent duodenal ulcer with crater by roentgenologic examination 42 months after vagotomy. The insulin test in this case gave negative results. In one patient with an excellent result five years after vagotomy, ulcer pain developed three years after vagotomy and a reactivated duodenal ulcer was found on roentgenologic examination. The insulin test was negative. However, he has responded to medical treatment and is asymptomatic at present.

Vagotomy and Gastric Resection.—One of the two living patients who had gastric resection in addition to

4. Weinstein, V. A.; Hollander, F.; Lauber, F. U., and Colp, R.: Symposium on Some Aspects of Peptic Ulcer; Correlation of Insulin Test Studies and Clinical Results in a Series of Peptic Ulcer Cases Treated by Vagotomy, *Gastroenterology* 14: 214 (Feb.) 1950.

5. "Good correlation" means that the patient had a negative result from an insulin test and no evidence of recurrent ulceration or a positive result from an insulin test with evidence of recurrent ulceration.

Priestley and Gibson⁷ found that, of 35 patients followed 5 to 10 years after excision of a gastrojejunal ulcer after gastroenterostomy with closure of the openings in the stomach and jejunum, 85.7% had recurrence of ulcer symptoms, and 31.4% required further surgery. From the results in the five cases in our series, it does not appear that vagotomy adds much to this procedure.

Priestley and Gibson⁷ made a similar 5 to 10-year follow-up study on 103 patients on whom gastric resection was performed for gastrojejunal ulcer after gastroenterostomy at a risk of 2.3%. Symptoms of recurrent ulcer developed in 12.6%, and further operative treatment was required in 5.8%. These results should be compared with the results of vagotomy alone for gastrojejunal ulcer after gastroenterostomy. In our study, we found that 12.8% of 34 patients had symptoms of ulcer, 2.9% required further operation, and 22.5% had persistent disturbances of motility one to five years after vagotomy. Gastric resection, therefore, appears to be the treatment of choice for this type of gastrojejunal ulcer.

Gastrojejunal ulceration after resection of at least 70% of the stomach always presents a most difficult therapeutic problem. Few patients have been traced after gastric re-resection for comparative purposes, but Priestley and Gibson⁷ did find that, of 11 such patients followed 5 to 10 years, only six were free of symptoms of ulcer. In our series of patients followed one to five years after vagotomy alone, 12.5% had recurrent symptoms of ulcer, 8.3% had required further operation, and 25% had persistent disturbances of motility. Thus vagotomy appears to be a sounder procedure in the treatment of gastrojejunal ulcer after gastric resection of at least 70% of the stomach than further resection of the stomach.

In cases in which gastrojejunal ulcer occurs after less than half to two-thirds of the stomach has been removed, we have performed further gastric resection in addition to vagotomy in selected cases. An insufficient number of cases of this type were available in our study or in the literature for us to settle the question of the advisability of combining these two procedures.

In seven of the eight cases of gastrojejuno-colic fistula in which vagotomy has been performed with or without the associated operative procedures described previously, the colonic fistula was closed. Interestingly enough, results one to five years after vagotomy have been excellent in six cases and poor in one case.

As judged by the clinical results, vagotomy by transthoracic or abdominal approaches differs little in effectiveness. If there is little doubt of the condition present and if additional procedures, such as excision of a perforating lesion or further gastric resection, are not considered possible or necessary, transthoracic vagotomy may be performed in cases of gastrojejunal ulcer after adequate gastric resection; yet it is not always possible to determine the amount of remaining stomach by roentgenologic examination after partial gastrectomy. That subdiaphragmatic division of the gastric vagus nerves can be carried out as completely as by supradiaphragmatic division has been stated by Dragstedt⁸ and proved by the anatomic dissections in 111 cadavers by Walters and co-workers.⁹

SUMMARY

A study has been made of the clinical features in 118 cases of gastrojejunal ulcer and in four cases of gastroduodenal ulcer in which vagotomy has been performed with or without other procedures. The transthoracic route was employed in 54 and the transabdominal route in 68 cases. Clinical results as of Jan. 1, 1951, have been determined by reexamination and laboratory studies one to five years after vagotomy in 13 cases and from replies to questionnaires in 84. In 41 of the 97 cases in which follow-up data were available, gastrojejunal ulceration had occurred after gastroenterostomy and in 53 after gastric resection. Gastroduodenal ulcer occurred after Billroth I resection in three cases.

Symptoms of gastrojejunal ulcer that were severe enough to warrant further surgery had developed after gastroenterostomy in an average of 9.3 years and after gastric resection in an average of 3.3 years. Thus, in order to include most of the recurrences, follow-up periods should differ for the two types of gastrojejunal ulceration.

Only 9.2% of the 54 patients who had moderate or massive hemorrhage before vagotomy and were followed one to five years after vagotomy had further hemorrhage.

The preoperative roentgenologic diagnosis of gastrojejunal ulcer was found to be correct in 67.2% of cases in which the transabdominal approach was used at operation.

Gastric acidity was reduced below preoperative levels one to five years after vagotomy in 85.3% of cases in which vagotomy alone had been performed for gastrojejunal ulcer after gastroenterostomy and in all cases in which it had been performed for gastrojejunal ulceration after gastric resection.

Vagotomy alone reduced gastric motility immediately in 54.6% of cases of gastrojejunal ulcer after gastroenterostomy and 42.1% of cases of gastrojejunal ulcer after gastric resection. One to five years after vagotomy alone, however, motility was reduced or absent in only 16.7% of the cases of gastrojejunal ulcer after gastroenterostomy and in 8.3% of the cases of gastrojejunal ulcer after gastric resection.

The over-all correlation of results of insulin tests with clinical results was excellent in 75% of all cases studied. However, in the cases in which recurrence of ulcer was proved, correlation of the results of insulin tests with clinical results was very poor. This indicates that the insulin test is a poor index of recurrent ulceration.

Vagotomy alone has produced excellent results in one to five years in 61.7% of 34 cases of gastrojejunal ulcer after gastroenterostomy and in 66.7% of 48 cases of gastrojejunal ulcer after gastric resection.

If the absence of symptoms of ulcer had been the sole criterion of an excellent result, the percentage of patients reporting excellent results would have been much higher. In our series of patients on whom vagotomy alone was performed for gastrojejunal ulceration, 88.2% of those who previously had had gastroenteros-

8. Dragstedt, L. R.: Section of the Vagus Nerves to the Stomach in the Treatment of Gastro-Duodenal Ulcer, *Minnesota Med.* 29: 597, 1946.

9. Walters, W.; Bradley, W. F.; Neibling, H. A.; Wilson, J. W.: Gastric Neurectomy for Gastric and Duodenal Ulcer: An Anatomic and Clinical Study, *Ann. Surg.* 126: 1, 1948.

tomy and 87.5% of those who previously had had gastric resection were free of symptoms of ulcer.

One-year to five-year results were excellent in five cases of gastrojejunal fistula treated by vagotomy with or without closure of the openings in the colon; one patient reported recurrent ulcer pain in two and one-half

years after operation. However, a larger series and longer follow-up periods are necessary before the effectiveness of vagotomy in the treatment of this condition can be evaluated. There is little evidence in our series that the results after transthoracic vagotomy differ from those after transabdominal vagotomy.

DIAGNOSIS AND TREATMENT OF ESOPHAGEAL DISEASES

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Tremendous strides have been made during the past decade in diagnosing and treating the various diseases that the esophagus is heir to. That such conditions are not rare, but are rather frequent, is evident by the voluminous literature that has accumulated recently on this subject. These diseases are of interest to the general practitioner and specialist alike, and it is with this thought in mind that the following discussion is presented.

ANATOMIC CONSIDERATIONS

Some points in the anatomy of the esophagus bear emphasis. It is well to remember that the esophagus per se is 10 in. (25.4 cm.) long, extending from the 6th cervical vertebra (cricoid cartilage level) to the 10th dorsal vertebra (esophageal hiatus level). The esophagologist, however, does not measure from the sixth cervical vertebra, but rather from the alveolar margin, which adds an additional 6 in. (15.24 cm.) to the actual length of the esophagus; thus he bases his report on a 16 in. (40.6 cm.) structure.

The esophagus has three normal curves, three physiological constrictions, and can be divided into three zones. Its three curves, or flexures, are placed in the following manner. In the neck the esophagus curves to the left; as it descends in the thorax, it curves to the right; and, as it approaches the esophageal hiatus, it curves again to the left. These flexures are of practical importance, since they may determine the proper side of approach. The three physiological constrictions are located (1) at the level of the cricoid cartilage (sixth cervical level), (2) at the arch of the aorta, and (3) at the esophageal hiatus. It is at these constrictions that the greatest amount of irritation takes place and the greater number of pathological lesions are observed. Most foreign bodies are impeded in their path downward at the first physiological constriction and are therefore found on a level with the sixth cervical vertebra. In locating a swallowed foreign body, it is all-important, therefore, to order a roentgenogram of the neck as well as of the chest.

The relation of the vagus nerves to the esophagus should be stressed, since these nerves may be involved or must be sacrificed in some esophageal procedures. Although much has been written recently regarding the anatomy of the vagi and although numerous patterns

have been described, in the main it may be stated that the left vagus nerve passes along the anterior aspect of the esophagus, intimately hugs the food pipe, and is the smaller of the two vagi. The right vagus passes posteriorly, does not hug the esophagus, and is larger.

To know the boundaries of the so-called esophageal triangle is to make identification and isolation of the supradiaphragmatic portion of the esophagus a simple and rapid maneuver. This anatomic triangle is bounded in front by the heart, behind by the descending aorta, and below by the diaphragm.

Almost every text, monograph, or recent article calls attention to the poor blood supply of the esophagus. I cannot agree with this teaching. To emphasize this point one needs only to divide the esophagus into upper (cervical), middle (thoracic), and lower (abdominal) parts. The upper part of the organ is supplied voluminously by the inferior thyroid artery; the middle, or thoracic, part is supplied by aortic, bronchial, and intercostal branches; the lower part is well supplied by the left gastric and the inferior phrenic arteries. On removal of the entire thoracic esophagus, both supra-aortic and infra-aortic portions, from its mediastinal bed, brisk, bright red arterial oozing is noted when the esophagus is transected at its entrance into the stomach. I feel, therefore, that much more can be expected of the esophagus in its ability to heal, particularly if careful sutures are placed and if tension is avoided.

CONGENITAL DEFECTS

Much has been learned recently about congenital atresias and tracheoesophageal fistulas, so that now they can be properly classified and treated. Various combinations and degrees of these anomalies are possible. The commonest such defect is one in which the proximal end of the esophagus terminates as a blind pouch and the distal end joins the trachea to form a tracheoesophageal fistula.

Such a defect is to be suspected if the newborn baby shows a symptom complex revealing the three "C's," namely, coughing, choking, and cyanosis. Especially is this true if there is an abnormal amount of drooling and rhinorrhea. These symptoms should suggest an impending surgical emergency. The roentgenologist is of inestimable value in determining the type and site of such lesions by merely noting the presence or absence of gas in the stomach and bowel and by injecting a small amount of iodized oil (lipiodol®) through a nasal catheter into the proximal portion of the esophagus (barium should never be used).

Read before the Section on Diseases of the Chest at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 15, 1951.

From the Departments of Surgery of the University of Illinois, Cook County Graduate School of Medicine, Cook County Hospital, American Hospital, and Alexian Brothers' Hospital.

The side of approach to atretic lesions and tracheo-esophageal fistulas is open to controversy. It is true that, if only a small narrow atretic portion in the esophagus exists, the right-sided approach is preferable. The reasons for this are that the arch of the aorta does not interfere with exposure, only the azygos vein need be ligated and severed to visualize the esophagus thoroughly, and an end to end anastomosis may be accomplished readily. However, if the atresia or the fistula involves a longer segment of esophagus, an end-to-end esophageal anastomosis cannot be accomplished. Thus, if one has utilized a left-sided approach, it is simple to open the diaphragm, mobilize the stomach, and perform an intrathoracic esophagogastrostomy. It should be remembered also that in the newborn and in the young the aorta is not the barricading impediment that it is in older persons, since in the young it can readily be retracted out of the way.

If a few of these pertinent facts are kept in mind, not every "blue baby" will be thought to have the tetralogy of Fallot, and an immediate and proper work-up will be instituted, thus saving many such children from unnecessary death.

ESOPHAGEAL HIATUS HERNIA

This hernia is a type of diaphragmatic hernia in which the upper part of the stomach herniates through the esophageal hiatus. The following three types of esophageal hiatal hernias have been described: (1) the paraesophageal type, in which the stomach herniates through the esophageal hiatus and lies parallel with an esophagus of normal length; (2) the sliding type, in which the stomach is herniated through the hiatus but has pushed an esophagus of normal length upward, thus rendering it tortuous; and (3) the hiatal hernia with a congenitally short esophagus, in which the upper part of the stomach is herniated through the hiatus because the esophagus has never attained its normal length.

The last-mentioned type can be diagnosed by the esophagologist when he records the appearance of gastric mucosa at an unusually high level, indicating a short esophagus. Hiatal hernias may be observed as a coincidental finding in taking gastrointestinal roentgenograms. Although many advocate leaving them alone, the danger of strangulation of such a herniated segment of stomach, with resulting putrid empyema and rapid death, must be kept in mind. Phrenicotomy might be the operation of choice in the aged patient with diaphragmatic hernia (fig. 1). By means of this method, which relaxes the diaphragm, strangulation and gangrene of the herniated contents might be prevented.

At times this type of hernia is associated with congenital absence of the diaphragm, and in such cases much of the gastrointestinal tract, spleen, and even the kidney have been found in the thoracic cavity.

Many patients with hiatal hernias complain of epigastric distress, bloating, belching, anorexia, loss of weight, and retrosternal pain. Such patients have been diagnosed erroneously as having disease of the gall-bladder, peptic ulcer, gastritis, or coronary disease. These errors can be avoided if the possibility of hiatal

hernia is kept in mind and if roentgenograms are taken with the patient in the Trendelenburg position, which would readily demonstrate herniation that might otherwise be overlooked. Unexplained secondary anemia should always make one suspicious of an overlooked diaphragmatic hernia.

The surgical repair of a paraesophageal hernia or a sliding type of hernia is simple, since all that is necessary is reduction of the herniated stomach and tightening of the esophageal hiatus. It is the hernia associated with a congenitally short esophagus that presents a problem. For such a lesion I have devised a procedure by which the hiatus is incised and enlarged and the defect increased. This is accomplished by herniating more stomach into the thoracic cavity, thus removing the pull on the congenitally foreshortened esophagus. The esophageal hiatus is then loosely sutured around the stomach.

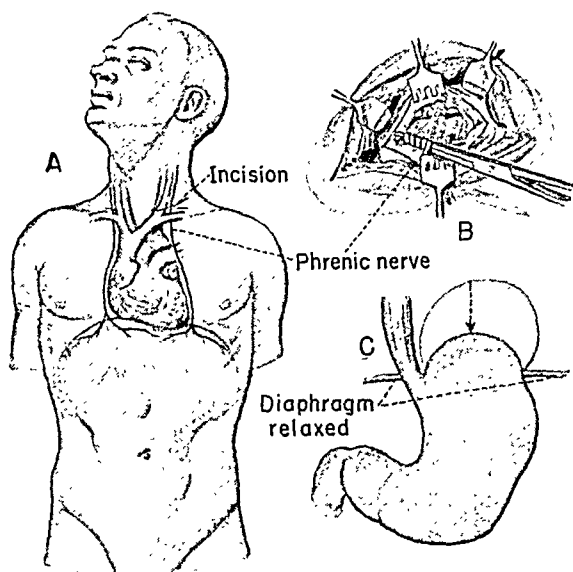


Fig. 1.—Phrenic avulsion for diaphragmatic hernia. A, the course of the phrenic nerve; B, avulsion of the nerve; C, relaxation of the left hemidiaphragm and reduction of the herniated stomach following phrenic nerve avulsion.

ESOPHAGEAL DIVERTICULA

The time-honored classification of diverticula into pulsion and traction types is still of value. The pulsion type of diverticulum occurs either in the neck (cervical) or immediately above the diaphragm (epiphrenic). The so-called traction type is usually located in the region of the tracheal bifurcation, where the chronically inflamed tracheal lymph nodes are found. These rarely produce symptoms, since they usually have a wide ostium that forms their neck. However, more important than the classification is appreciation of the pathological physiology that underlies the formation of this condition. It is believed that one of the prerequisites for the pulsion type is a weakness in the muscular wall, which permits herniation of the mucosa through the weak part and results in a diverticulum. No symptoms are produced as long as the opening into the diverticulum is large; however, as food slowly packs into the diverticulum, the latter increases in size and drops downward. This process con-

tinues until the weighted sac hangs downward and produces pressure on the esophagus, obstructing it. It should be noted that in such a far-advanced stage food has easier access to the diverticulum than to the esophageal lumen proper. Dysphagia is the outstanding complaint, and diverticulitis, perforation, and mediastinitis are the commoner complications.

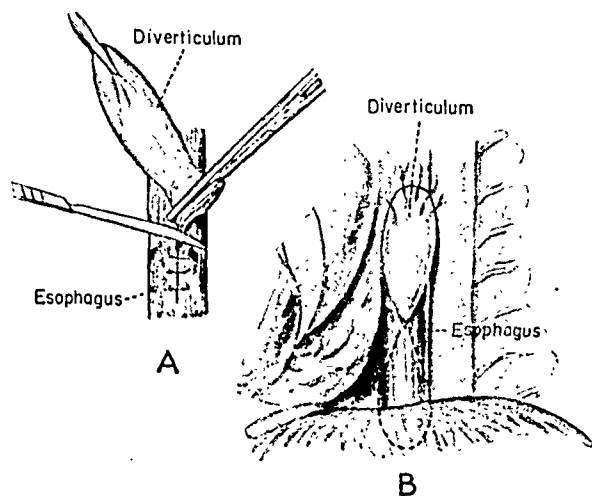


Fig. 2.—A, diverticulectomy and B, diverticulopexy.

In this day of chemotherapy, improved surgical technique, modern anesthesia, and proper postoperative care, the one stage diverticulectomy is preferred over the two stage procedure. Although removal of the diverticulum is preferred, diverticulopexy still has its place (fig. 2). The latter procedure, in which the diverticulum is dissected free and stitched upward to the surrounding structures, is reserved for the poor risk patient with marked symptoms. When this has been done, food does not have access to the downward-hanging diverticulum, and thus the symptoms are relieved.

PORTAL HYPERTENSION

A ruptured esophageal varix causes a true surgical emergency that taxes the diagnostic ability, skill, and judgment of the surgeon. This condition results from the increased pressure in the portal system and is almost always observed at the lower end of the esophagus (recent studies reveal, however, that varices may occur in any part of the esophagus). Portal hypertension may be due to intrahepatic or extrahepatic causes. The usual condition causing intrahepatic block is cirrhosis of the liver. Extrahepatic block may be due to phlebitis, thrombosis, fibrous stenosis, or cavernomatous transformation of the portal vein; it may be congenital or acquired.

One does not refer to Banti's disease in these modern times, but rather to Banti's syndrome. This is characterized by splenomegaly, anemia, esophageal varices, ascites, and leukopenia. The syndrome has been produced experimentally by Whipple, who blocked the portal vein. If the block is due to an intrahepatic lesion, the liver function tests will give positive results; whereas if the portal block is extrahepatic, the results of these tests are usually negative. If the condition is in a quiescent stage, it may be safe to take an esophagram, which will reveal the pathognomonic "beaded" appearance at the lower end of the esophagus.

Since hemorrhage from a ruptured esophageal varix may be fatal, definite measures must be taken to prevent recurrence. Some of the therapeutic procedures advocated are injection of the varix with sclerosing agents, tamponade with oxidized cellulose (oxycel®) or absorbable gelatin sponge (gelfoam®) through the esophagoscope, ligation of the coronary vein, esophagogastric resection to remove the "pile bearing" area, and various forms of portacaval shunts. Garlock has recently advocated mediastinal packing for such profuse hemorrhage.

Portacaval shunts have attained a certain degree of popularity in the past few years, and various types of anastomoses have been attempted in order to shunt the blood from the portal to the caval system. It is my opinion that, rather than the time-honored end-to-side portacaval shunt (Eck fistula), a lateral anastomosis between the portal vein and the inferior vena cava will prove to be the method of choice. This is accomplished best through a right thoracotomy incision in which the costal arch is divided, making it possible to dislocate the right lobe of the liver into the right thoracic cavity. When this approach is used, the portal vein and the inferior vena cava practically approximate themselves, thus avoiding the necessity of dissecting out the common duct and the hepatic artery. It seems preferable also to permit some portal blood to continue through the liver, rather than make a complete division of the portal vein. Only time will tell the efficacy of these measures.

Recently Rienhoff has advocated ligation of the hepatic artery close to its point of origin as a palliative method of controlling the complications associated with portal hypertension (fig. 3).

CARDIOSPASM (ACHALASIA) OF ESOPHAGUS

Cardiospasm is a condition in which there is dilatation, hypertrophy, and tortuosity of the esophagus associated with an obstructed esophageal hiatus. Theories

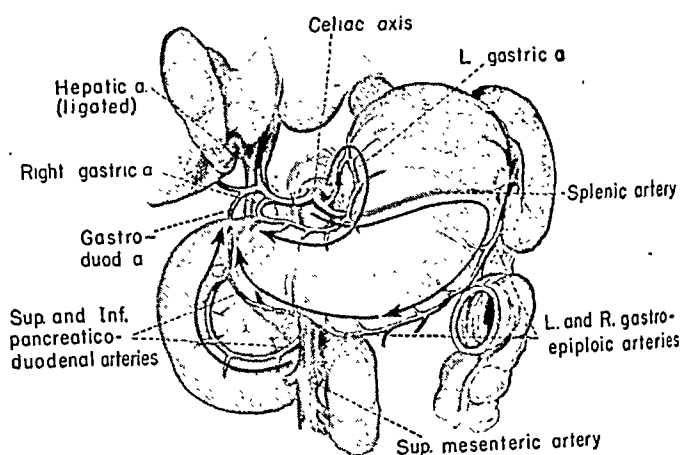


Fig. 3.—Ligation of the common hepatic artery for portal hypertension. The collateral circulation is indicated by arrows.

as to its production are numerous and will not be discussed here. This condition is twice as common in women as in men, and in a rather large percentage of patients a history of emotional strain or psychic trauma can be elicited.

This condition has been divided into types or stages. The early case shows a fusiform appearance; the mod-

erately advanced case, a flask-shaped appearance; and the far advanced case, the true sigmoid variety. The outstanding symptoms are dysphagia, regurgitation, and pain. Complete esophageal obstruction for varying periods has been noted, even to a point where the patient cannot swallow his own saliva. The pain is usually retrosternal and varies from mild to severe. Morphine addiction has resulted from this condition.

The roentgenogram is of particular help in diagnosing *cardiospasm*. Recently Kramer and Ingelfinger described the methacholine (mecholy[®]) test as an aid to the diagnosis of *cardiospasm*. When methacholine, a parasympathomimetic drug, is injected into a normal person, there is only a slight increase in tone and magnitude of esophageal contractions; however, in patients with *cardiospasm* marked esophageal spasm and contractions follow administration of the drug. Complications that may be associated with the condition are bronchitis, bronchiectasis, and pulmonary abscess. All these may result from aspirated material regurgitated from the esophagus.

Medical management includes psychotherapy, antispasmodics, and dilatation. Only 10% of these patients require surgical treatment; in the remaining 90% the condition can be controlled by the other forms of therapy mentioned. Surgically, many types of procedures have been advised, which include cardioplasties, cardiomyotomies, resections, and anastomoses.

CARCINOMA OF ESOPHAGUS

No longer is a defeatist attitude assumed in cases of carcinoma of the esophagus. What was considered a hopeless and inoperable condition only a decade ago presents at least a worth-while challenge to the surgeon of today. If present impressions are correct, the over-all outlook and prognosis for the patient with carcinoma of the esophagus is better than the 5%, five year "cure" prognosis for patients with carcinoma of the stomach.

It is of practical value to divide the esophagus into zones. Many such divisions have been described. One that has served me well divides the organ into three zones, namely, an upper (zone 1), which extends from the beginning of the cervical esophagus to the manubrium sterni; a middle (zone 2), which extends from the manubrium sterni to the inferior pulmonary ligament; and a lower (zone 3), which extends from the inferior pulmonary ligament to the esophagogastric junction.

Early diagnosis is of paramount importance in cases of this type of carcinoma, since it is by this means that the survival rate can be increased. One often hears mention of a "change in stool habit" as a probable symptom of carcinoma in the lower intestinal tract; in like manner it may be stated that any persistent change in the swallowing habit is an indication of carcinoma of the esophagus, until proved otherwise. Were this dictum to be heeded and such cases further investigated by means of esophagoscopy and roentgen study, many esophageal neoplasms would be operated on earlier.

TREATMENT

Needless to say, preoperative and postoperative therapy for these patients is of the utmost importance, and much has already been written concerning these phases.

For lesions located in zone 1 the Wookey procedure¹ has been used, especially for a tumor situated in the cervical portion of the esophagus. Recently, however, lesions involving the superior mediastinal segment of the esophagus as well as the cervical part have been approached by a more radical procedure, which removes the thoracic portion of the esophagus and most of the cervical portion. This is accomplished through a thoracic phase of the operation and a cervical phase. The operation is completed by an intracervical end-to-side esophagogastrostomy. In placing the mobilized stomach in the neck, the surgeon may find that the thoracic inlet impinges on the stomach. If this is the case, it may be necessary to remove the inner half of the clavicle and the first rib. Whether the mobilized stomach should be placed behind or in front of the arch of the aorta is a moot question and must be decided on by the surgeon at the time of operation.

Lesions of zone 2, or those which involve most of the thoracic portion of the esophagus, are removed by a rather standardized procedure, in which a wide esophageal resection is accomplished, followed by an end-to-side supra-aortic esophagogastrostomy or esophagojejunostomy. When the jejunum is used, it may be necessary to do a Roux Y-anastomosis or some modification thereof.

Lesions of zone 3 include not only the lower end of the esophagus but the gastric cardia as well. I prefer a thoracolaparotomy incision, in which a left rectus incision extends across the left costal arch, dividing it and then continuing into the eighth intercostal interspace. The diaphragm is divided to and through the esophageal hiatus, and the esophagus is mobilized from the aortic arch to its entrance into the stomach; the latter is then mobilized to the pylorus. The right gastric and gastroepiploic arteries should be left intact. An esophagogastric resection is then accomplished and is followed by an end-to-side esophagogastrostomy. If necessary, the spleen and part of the pancreas are removed.

In most of my esophageal operations water seal drainage is preferred, and a Levine intragastric tube is permitted to remain in place for the first three postoperative days. I cannot subscribe to the teaching that these tubes may be harmful. Routine portable roentgenograms are taken 24 hours after operation to determine the pulmonary status.

PALLIATIVE PROCEDURES

Although the primary lesion may be extensive or may even show distant metastases, it is always worthwhile to attempt a palliative resection, thereby improving the patient's general condition and sense of well being. This is explained by the fact that infection is reduced and anemia is corrected. In the event that it is impossible to remove the primary growth, some short circuiting procedure, such as an esophagogastrostomy or an esophagojejunostomy, may make the patient's remaining days more comfortable.

1. In the Wookey procedure a skin flap is made from the skin of the neck. This is placed under the mobilized cervical portion of the esophagus and tumor. Some days later the tumor and adjoining esophagus are removed, and the esophageal defect is bridged by the tube formed from the previously made flap.

RUPTURE OF ESOPHAGUS

Both spontaneous and traumatic rupture of the esophagus have been described in the literature. A spontaneous rupture is an interesting lesion and is not so extremely rare as it was formerly thought to be. If one has the condition in mind, it should be possible to diagnose it preoperatively. It is found most frequently in male patients who are victims of alcoholism and is associated with a preliminary severe bout of vomiting; this is followed by agonizing pain, which may be either thoracic or abdominal. The patient usually goes into rapid and profound shock. This condition cannot be confused with a ruptured peptic (gastric or duodenal) ulcer, since with the ruptured ulcer the pain appears first and is followed by vomiting; whereas with the spontaneous rupture, vomiting comes first and is followed by pain. The ruptured esophagus is associated frequently with surgical emphysema, which can be felt in the neck. Whenever such emphysema is noted, one should think immediately of spontaneous esophageal perforation and verify this with a flat roentgenogram, which will reveal a spontaneous hydropneumothorax. Aspiration of the chest has been done in some cases, resulting in the discovery of food particles or vomitus. Formerly the mortality was thought to be 100%; however, with early diagnosis and modern surgical therapy the outlook is much better today, and some patients are definitely being saved.

MEDIASTINITIS

Perforation of the esophagus may result in a serious condition—mediastinitis. Malignant tumors or foreign bodies are the two main causes of perforation. Since carcinoma develops gradually, it does not give rise to as extensive an infection of the mediastinum as do other lesions.

Perforations caused by foreign bodies are of more practical importance. At present it is felt that mediastinal infections that extend deeper than the fourth or the fifth thoracic vertebra cannot be adequately drained by means of cervical mediastinotomy and must be treated by posterior mediastinotomy. Chemotherapy is an all-important adjunct for this type of infection.

BENIGN TUMORS

Benign tumors of many types have been found in the esophagus, the commonest of which are lipomas and myomas. Owing to the constant effect of swallowing, such tumors have a tendency to become tremendously elongated and pedunculated. They have been known to be coughed up and to appear in the patient's mouth. If this occurs, it may be possible to remove the lesion by means of a snare passed orally. If the tumor, however, is lower down, esophagotomy with removal of the tumor and primary closure of the esophagus is the treatment of choice.

ESOPHAGITIS

The important subject of esophagitis is coming into its own today; this is probably one of the most overlooked clinical entities. Numerous editorials and articles on this subject are appearing in current literature, and its importance is being stressed. It is suspected in cases

associated with heartburn, retrosternal pain, dysphagia, peptic ulceration, mediastinitis, dilatation of the esophagus, and perforation with putrid empyema. The esophagologist can usually make a definite diagnosis if the condition is only suspected. The treatment is both medical and surgical.

In the far-advanced case with marked cicatricial stenosis and almost complete obstruction, the surgical treatment taxes the experience and skill of the surgeon. In a patient recently operated on by me it was necessary to create a temporary esophageal fistula over a T-tube to overcome the stenosis and permit healing.

It is impossible to mention in this paper every aspect of esophageal pathology. Only the commoner and more frequent conditions have been stressed. The esophagus has been just as much a "hermit" as the pancreas; however, recently it has been brought within reach of the well-equipped and well-trained general practitioner and specialist alike. That this organ is accessible to modern diagnostic and therapeutic procedures is due to the efforts of such men as Franz Terek, Sauerbruch, Garlock, Sweet, Nissen, and others too numerous to mention. Their contributions have enabled the modern surgeon to save many lives that were doomed a decade ago. Today the future for esophageal therapy is most promising.

SUMMARY

The commoner pathological conditions that affect the esophagus have been discussed, and their treatments have been evaluated. The importance of physiopathology as an aid to early diagnosis has been stressed. The advent of improved diagnostic methods, modern anesthesiology, chemotherapy, skillful surgical technique, and proper preoperative and postoperative care has brought the esophagus into the realm of therapeutic safety.

25 E. Washington St.

Evaluation of Antacids.—Calcium carbonate appears to be the most effective of the many antacids in current use. In hourly doses of 2 or 4 gm., together with milk and cream and atropine, 1.0 mg. two to four times daily, calcium carbonate usually maintains the pH of the gastric contents between 4.0 to 5.5 in patients with duodenal ulcer; it does not cause alkalosis, as has been assumed, and its constipating effect can be corrected with proper substitution of laxative antacids. This regimen, however, is effective only during the period of administration; it does not control the excessive nocturnal gastric secretion of duodenal ulcer. The continuous intragastric drip is perhaps more effective for this purpose, but its applicability is limited. Aluminum hydroxide, magnesium trisilicate or tribasic calcium phosphate in large quantities diminish but do not completely eliminate the free acidity; their neutralizing effect is much less or nil when administered at long intervals and in small amounts, as is the custom of some clinicians. . . . The antacid efficiency of sodium carboxymethylcellulose in man remains to be determined. Protein hydrolysates are less effective than calcium carbonate even when administered in large amounts, and they provoke a secondary rise in secretion exceeding original levels. The neutralizing capacity of available resins *in vivo* is not impressive. Detergents such as sodium alkyl sulfate do not alter the pH of the gastric contents, and their antipeptic action in man is insignificant. Mucin has little neutralizing value.—Joseph B. Kirsner, M.D., Walter L. Palmer, M.D., Erwin Levin, M.D., and Arthur P. Klotz, M.D., *Gastric Antacid and Anti-Secretory Drugs: A Survey Based Primarily on Their Effects Upon Gastric Secretion In Man*, *Annals of Internal Medicine*, October, 1951.

VALUE OF CARDIAC FUNCTION TESTS IN INDUSTRY

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and

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Since the diagnosis of heart disease and the evaluation of cardiac function cannot always be made by the routine clinical methods, dependable functional tests of the heart are definitely necessary. Cardiovascular disease is the leading cause of death in the country today. This is, of course, related to the increasing numbers of aged in our population. In modern industrial plants especially, therefore, is the need for accurate diagnostic and functional tests of the heart now most apparent—including tests of laborers, white collar workers, and executives. The continuing partial disability of workmen with angina pectoris due to coronary disease, chronic congestive heart failure, or even cardiac neurosis is much more important than is the occasional dramatic attack of acute coronary occlusion or insufficiency among apparently healthy airplane pilots while in flight.

From the standpoint of the nation's needs, the physician in industry must assume the responsibility for ferreting out previously undetected cardiac disease from among the employees or executives of his concern. Executives, especially, are generally considered to be likely victims of unsuspected coronary artery disease and of death due to this cause. From a purely economic standpoint, furthermore, functional tests are needed for evaluating and processing disability claims in life insurance and workmen's compensation cases and for determining the time for retirement of the increasing numbers of aged employees. Cardiac function tests, therefore, are today at least as vital in industrial medicine as they have been in the past in private practice.

The following four cardiac function tests will be discussed: (1) the "2-step" exercise electrocardiogram, (2) the anoxemia (10% oxygen) test, (3) the ballistocardiogram, and (4) the Krasno-Ivy nitroglycerin flicker test. The technique, safety, and diagnostic value of these tests will be considered in detail.

"2-STEP" EXERCISE ELECTROCARDIOGRAM

In 25 to 37% of the patients with coronary artery disease, the results of all routine investigations—physical examination, cardiac fluoroscopy, teleroentgenogram of the chest, and 12 lead, resting electrocardiogram—may be normal.¹ There is, therefore, an increasing trend toward the use of stress tests of the heart, in order to obtain some possible objective evidence of the presence of organic heart disease.

In 1929 the "2-step" exercise procedure was devised by Enid T. Oppenheimer and Master² as a practical test of circulatory fitness. After thousands of trials, tables were formulated that prescribed the standard number of trips patients should make, depending on their age, sex, and weight. The tables were at first based on the response of the blood pressure and pulse to exercise. Later, electrocardiographic changes following standard exercise were used as the test for coronary insufficiency.³

Method.—The "2-step" test is performed on a patient only if the usual 12 lead, resting electrocardiogram is normal. The patient climbs the "2-step" stairs (each step is 9 in. [22.9 cm.] high) with the four electrodes left in place (fig. 1). Standard leads 1, 2, and 3 and a precordial lead, V_4 or V_5 (with the tallest, widest R wave), are taken routinely. In the standard or single test, the required number of ascents for each patient (complete trips over the steps in one direction) is determined from table 1 or 2; the test is performed in one and one-half minutes. After the exercise is completed, the patient returns to his original resting position, sitting or recumbent, and the electrocardiogram is taken immediately,

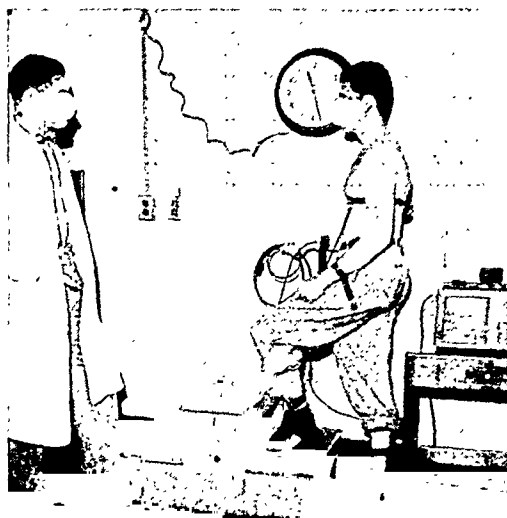


Fig. 1.—Patient, with electrodes attached, about to perform "2-step" exercise test.

two minutes and six minutes later. Dizziness may be avoided by having the patient change his direction after the completion of every trip, i. e., turning toward the examiner each time. If the single test is normal, the double "2-step" test is performed, at least one hour later. This consists of making twice the number of standard trips in three minutes. One-third of the patients with abnormal double tests had normal single tests; the single "2-step" test is performed first, for obvious reasons of safety.

From the Cardiographic Department of the Mount Sinai Hospital.
Read before the Section on Preventive and Industrial Medicine and Public Health at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 14, 1951.

1. White, P. D.: Heart Disease, New York, The Macmillan Company, 1944, ed. 3, p. 827. Master, A. M.: The Two-Step Exercise Electrocardiogram: Test for Coronary Insufficiency, *Ann. Int. Med.* 32: 842, 1950.

2. Master, A. M., and Oppenheimer, E. T.: Simple Exercise Tolerance Test for Circulatory Efficiency with Standard Tables for Normal Individuals, *Am. J. M. Sc.* 177: 223, 1929.

3. Master, A. M.; Friedman, R., and Dack, S.: The Electrocardiogram After Standard Exercise as a Functional Test of the Heart, *Am. Heart J.* 24: 777, 1942.

Criteria for abnormal "2-step" tests include: (1) RS-T segment depression (greater than 1/2 mm.) below the isoelectric (P-R) level; (2) partial or complete inversion of a T-wave (except in lead 3); (3) transient arrhythmias, conduction defects, or large Q-waves. These changes are similar to those found during spontaneous episodes of angina pectoris. The precordial leads were found to be the most sensitive (V₄ or V₅). If the alterations persist for longer than six minutes, the tracings are repeated until the record returns to normal. It is

anoxia and ischemia of the subendocardial layer of the myocardium, owing to acute coronary insufficiency, induced by the exercise. The safety of the "2-step" exercise electrocardiogram test is proved by the absence of untoward reactions in thousands of patients tested—the customary precautions and standardized technique being used.

Follow-Up Studies.—A follow-up study from one to five years' duration, of 200 cases is reported (100 cases with abnormal "2-step" exercise electrocardiograms and

TABLE 1.—Standard Number of Ascents for Males*

Weight (Lb.)	Age in Years											
	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64
40-49	35	36	..	..	..	..	..	..	..	..	..	..
50-59	33	35	32	..	..	..	..	..	..	..	..	..
60-69	31	33	31	..	..	..	..	..	..	..	..	..
70-79	28	32	30	..	..	..	..	..	..	..	..	..
80-89	26	30	29	29	29	29	27	27	26	25	25	24
90-99	24	29	28	28	28	27	27	26	25	25	24	23
100-109	22	27	27	28	28	27	26	25	25	24	23	22
110-119	20	26	26	27	27	26	25	25	24	23	23	22
120-129	18	24	25	26	27	26	25	24	23	23	22	21
130-139	16	23	24	25	26	25	24	23	23	22	21	20
140-149	..	21	23	24	25	24	24	23	22	21	20	20
150-159	..	20	22	24	25	24	23	22	21	20	20	19
160-169	..	18	21	23	24	23	22	22	21	20	19	18
170-179	..	..	20	22	23	23	22	21	20	19	18	17
180-189	..	..	19	21	23	22	21	20	19	19	18	17
190-199	..	..	18	20	22	21	21	20	19	18	17	16
200-209	..	..	..	19	21	21	20	19	18	17	16	15
210-219	..	..	..	18	21	20	19	18	17	17	16	15
220-229	..	..	..	17	20	20	19	18	17	16	15	14

* From Am. Heart J. 10: 497, 1935.

TABLE 2.—Standard Number of Ascents for Females*

Weight (Lb.)	Age in Years											
	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64
40-49	35	35	33	..	..	..	..	..	..	..	..	..
50-59	33	33	32	..	..	..	..	..	..	..	..	..
60-69	31	32	30	..	..	..	..	..	..	..	..	..
70-79	28	30	29	..	..	..	..	..	..	..	..	..
80-89	26	28	28	28	28	27	26	24	23	22	21	21
90-99	24	27	26	27	26	25	24	23	22	22	21	20
100-109	22	25	25	26	26	25	24	23	22	21	20	19
110-119	20	23	23	25	25	24	23	22	21	20	19	18
120-129	18	22	22	24	24	23	22	21	20	19	19	18
130-139	16	20	20	23	23	22	21	20	19	19	18	17
140-149	..	18	19	22	22	21	20	19	19	18	17	16
150-159	..	17	17	21	20	20	19	19	18	17	16	15
160-169	..	15	16	20	19	19	18	18	17	16	16	15
170-179	..	13	14	19	18	18	17	17	16	16	15	14
180-189	..	..	13	18	17	17	17	16	16	15	14	14
190-199	..	..	12	17	16	16	16	15	15	14	13	13
200-209	..	..	..	16	15	15	15	14	14	13	13	12
210-219	..	..	..	15	14	14	14	13	13	13	12	11
220-229	..	..	..	14	13	13	13	13	12	12	11	10

* From Am. Heart J. 10: 497, 1935.

not the purpose of this objective test to induce chest pain; the appearance of electrocardiographic alterations is, moreover, independent of the occurrence of pain or pressure. The test should not be performed within one hour after a meal or other exercise. Smoking and drugs, such as digitalis and nitroglycerin, have an influence on the result of the test. Cardiac enlargement or heart failure are definite contraindications to it. The "2-step" test is simple, safe, standardized, and employs climbing, a form of exercise to which every patient is accustomed. The RS-T segment and T-wave alterations in abnormal tests are related to transient

100 with normal exercise electrocardiograms, in order to prove the practical value of this procedure. Cases with Normal Tests: In the group of 100 consecutive cases with normal tests, there were 83 men and 17 women, ranging in age from 21 to 71 years. The follow-up studies extended over a period of five years; the majority were studied for at least two years. The largest number of patients (41) were in the 40 to 49 year age group. Sixty-eight of the 83 men were employed—39 were professional people or executives, 25 were white collar workers, and 4 were laborers. Of the 17 women, 14 were housewives, and 3 were gainfully em-

ployed. The chief presenting symptoms were chest pain or pressure in 62, hypertension in 13, and arrhythmias in 8; 8 others had miscellaneous symptoms. The remaining nine were asymptomatic and came for routine examination.

The follow-up study of this group of patients confirmed the belief that the presence of coronary insufficiency could practically be excluded, i. both the single and double "2-step" tests were normal. All of these 100 patients are alive today. In only one instance did a coronary episode occur after the exercise tests had been found to be normal. This was in a woman in whom acute coronary occlusion developed three years after the initial test. Among hundreds of other patients also observed, spontaneous coronary disease episodes very rarely occurred within one year following normal tests. Thus, the diagnostic and prognostic value of normal "2-step" exercise electrocardiograms is established. This

TABLE 3.—Normal Single and Double "2-Step" Tests (One Hundred Consecutive Cases)

Final Diagnosis	Men	Women	Total
Normal	3	2	5
Functional	50	6	56
Hypertension	25	4	29
Previous coronary occlusion.....	4	2	6
Later coronary occlusion.....	0	1*	1
Rheumatic heart disease.....	1	2	3
Total.....	83	17	100

* Three years later.

TABLE 4.—Normal Single and Double "2-Step" Tests (Sixty-Two Cases of Chest Pain or Pressure)

Associated Diagnosis	Men	Women	Total
Gallbladder.....	4	1	5
Arthritis.....	7	2	9
Hiatus hernia.....	3	1	4
Ulcer.....	2	0	2
None.....	35	7	42
Total.....	61	11	62

is in sharp contrast to the other commonly employed tests for coronary insufficiency, e. g., the anoxemia test (see below), in which only abnormal tests are of diagnostic importance.

The final diagnoses in this normal group are listed in table 3. Sixty-one patients were found to be normal, or to have some functional heart disturbance. Six patients had had a previous coronary occlusion; their excellent clinical recovery was confirmed by the normal exercise electrocardiogram and by later follow-up studies. Since normal "2-step" tests practically exclude coronary insufficiency, further studies were undertaken of the 62 patients with normal tests having undiagnosed chest pain. In approximately one-third of these, gallbladder disease, arthritis, hiatus hernia, and peptic ulcer were discovered to be the underlying cause for the symptoms (see table 4). Thus, B. D., a white woman, 63, gave a history of recent severe, though atypical, chest pain. All the cardiac findings were normal, including a single and double "2-step" test (fig. 2). Further investigation revealed a far-advanced spondylitis, with marked lipping and bridging of the thoracic vertebrae, to be the underlying disease (fig. 3). A three-year follow-up study of this patient has revealed no cardiac episode. Such cases

further confirm the diagnostic and prognostic value of normal "2-step" tests.

Cases with Abnormal Tests: Abnormal "2-step" exercise electrocardiograms, single or double, are definite evidence of the presence of coronary insufficiency. They may, at first, be the only objective finding in many

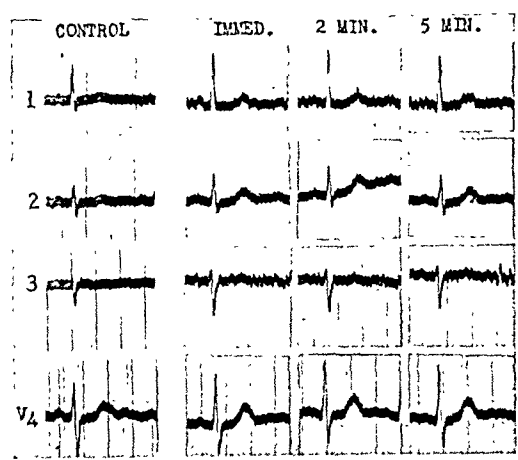


Fig. 2.—Double "2-step" test of B. D., a white woman, 63, with a typical severe chest pain. Control resting electrocardiogram and double "2-step" test is normal. Spondylitis was found to be cause of patient's symptoms.

cases of angina pectoris. Abnormal electrocardiographic findings after exercise, however, are not specific for coronary artery disease; rheumatic, syphilitic, or congenital heart disease or severe anemia may be the underlying organic condition. Moreover, the "2-step" test is abnor-

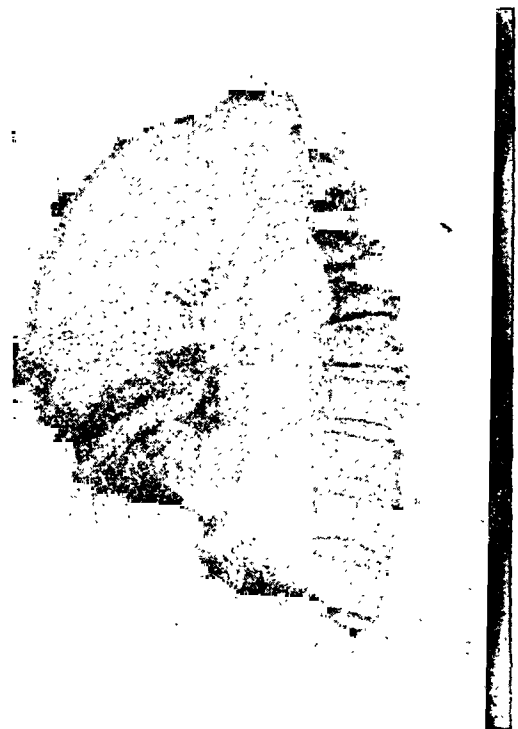


Fig. 3.—Same patient as in figure 2. Lateral chest roentgenogram revealing evidence of marked spondylitis.

mal in approximately 6 to 8% of normal persons. Patients with anxiety states or neurocirculatory asthenia may, likewise, have abnormal exercise tests. Thus, the insufficiency may be on a purely functional rather than organic basis. Unless this is borne in mind, numerous

patients may erroneously be labeled "cardiacs" and unnecessarily be limited in activity for the remainder of their lives. The differentiation between the functional and organic can usually be made on clinical grounds alone. In the hope of finding a further means of differentiating between the two, however, we have used dihydroergocornine (DHO-180), a "sympatholytic" agent.⁴ In most patients with functional heart disturbances, this drug prevents the appearance of electrocardiographic abnormalities after the "2-step" test. Moreover, in most patients in whom the "2-step" test remained abnormal after use of dihydroergocornine, follow-up studies revealed definite evidence of the presence of coronary disease. Ergotamine, which had previously been used as an aid in this differential diagnosis, has been found to be too dangerous.

The group of 100 consecutive cases with abnormal single or double "2-step" tests consisted of 71 men and 29 women, ranging in age from 25 to 71 years. The largest number of patients (44) were in the 50 to 59 year age group. The follow-up studies extended over a period from six months to four years; most of the pa-

tion. However, no RS-T segment deviations or T-wave inversions were seen in their resting electrocardiograms. In 14 of this group additional coronary attacks occurred.

The remaining 50 patients had had no previous spontaneous coronary episodes but had abnormal "2-step" tests. Twenty-one of these subsequently suffered from coronary occlusion or insufficiency—e. g., S. N., a 38-year-old white man, a dark, nervous gypsy (fig. 4), complained of severe heaviness across the chest for the preceding three months (in 1949). The chest pressure was unrelated to effort. Physical examination, chest roentgenogram and fluoroscopy, and a 12 lead, resting electrocardiogram revealed no abnormalities. The single "2-step" test was abnormal, showing ventricular premature beats and RS-T depressions in leads V₁ and 2. Three weeks after the "2-step" test had been made, an acute coronary occlusion with anterior wall infarction developed. After this episode the patient made a slow recovery. Although he still suffers from a severe anginal syndrome (relieved by use of nitroglycerin), the resting electrocardiogram is again within normal limits. However, the "2-step" test is abnormal whenever essayed.

Thus, in 71 of 100 cases with abnormal single or double "2-step" tests, the follow-up investigation has revealed evidence of organic coronary artery disease. In

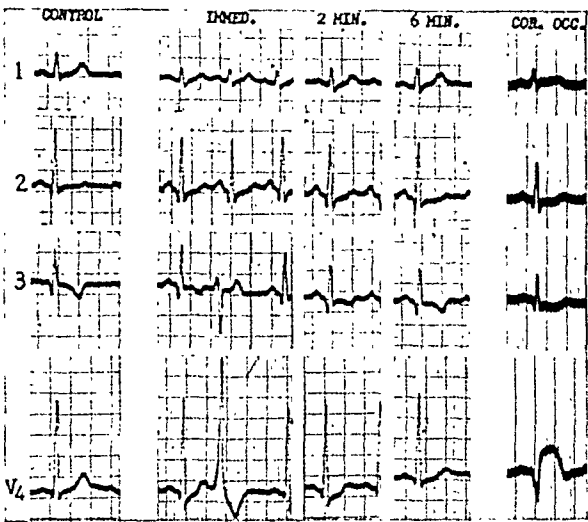


Fig. 4.—Single "2-step" test of S. N., a white man, 38, with angina pectoris unrelated to effort for three months. Control resting electrocardiogram is normal. Single "2-step" test is abnormal, with RS-T segment depressions in leads V₁ and 2 and ventricular premature beats after exercise. Three weeks later acute anterior infarction developed.

tients were reexamined at intervals for at least two years after the initial "2-step" test had been done. Sixty-one of the 71 men were employed—35 were professional persons or executives, 15 were white collar workers, and 11 were laborers. Twenty-four of the 29 women were housewives, and the remainder were paid workers. The chief presenting symptoms were chest pain or pressure in 76, hypertension in 8, arrhythmias in 9, and miscellaneous complaints in the remainder.

The results of the follow-up study in this group are listed in table 5. In 50 of the patients there had been definite electrocardiographic evidence of previous coronary episodes, either occlusion or insufficiency. All these patients had normal resting electrocardiograms at the time of their initial abnormal "2-step" test, though several displayed Q-waves of previous myocardial infar-

TABLE 5.—Abnormal Single or Double "2-Step" Tests (One Hundred Consecutive Cases)

Final Diagnosis	Men	Women	Total
Previous coronary occlusion.....	11	2	13
Later coronary occlusion.....	4	1	5
Previous coronary insufficiency.....	27	10	37
Later coronary insufficiency.....	12	4	16
Coronary disease (undetermined).....	17	12	29
Total.....	71	29	100

seven of these cases the patient has died as a result of coronary episode. The group of 29 cases of as yet unconfirmed coronary disease include only a very few cases in which the clinical diagnosis was neurogenic or functional coronary insufficiency. The follow-up study of these 200 cases, with normal and abnormal "2-step" tests, is further evidence of the value of the exercise electrocardiogram as a functional test of the heart.

ANOXEMIA (10 PER CENT OXYGEN) TEST

For four years we have performed the anoxemia (10% oxygen) test routinely for the purpose of critically evaluating it. We have compared the results of over 300 anoxemia tests with those of the single and double "2-step" tests in the same persons.

Method.—The following description of the anoxemia test is given by Levy.⁵ The resting electrocardiogram is recorded after the patient has been at bed rest for at least 30 minutes. As in the "2-step" test, the three standard limb leads and one precordial lead are used routinely. After the control record is taken, the patient breathes from a tank containing a mixture of 10% oxygen and 90% nitrogen. The mixture is passed through a water bottle before it reaches the patient. A flutter valve arrangement prevents rebreathing. The patient usually inhales the mixture for a period of 20 minutes; a tank of 100% oxygen is then substituted for the one with the low oxygen mixture for one minute or longer. The procedure may be stopped earlier if the test is abnormal

4. Porty, L.; Aral, H. S., and Master, A. M.: Dihydroergocornine in Differential Diagnosis of Functional Heart Disturbances and Organic Heart Disease, J. Mt. Sinai Hosp. 17: 26, 1950.
5. Levy, R. L.: Clinical Aspects of Coronary Insufficiency, Am. J. Med. 4: 89, 1948.

or if chest pain, pressure, or a severe reaction should occur. Electrocardiographic tracings are taken 10 and 20 minutes after the test is begun.

We have modified the procedure, as described above, to some degree. Instead of the precordial lead 4F, we have substituted lead V₄. The control record is repeated after the application of the mask, since a resultant fear and fright may produce pronounced electrocardiographic alterations.⁶ If the tracing is then still normal, the test is begun. Electrocardiograms are taken at 5 minute intervals during the 20 minute period of breathing 10% oxygen. A direct writing electrocardiogram machine has been found invaluable, since with it the procedure may be stopped as soon as the test is found to be abnormal.

Criteria for an abnormal anoxemia test include: 1. The arithmetic sum of the RS-T segment deviations in all four leads (1, 2, 3, and 4F) must be greater by 3 mm. or more than that of the control record. 2. There must be partial or complete reversal in the direction of the T-wave in lead 1, accompanied by an RS-T deviation of 1 mm. or more in this lead. 3. There must be complete reversal in direction of the T-wave in lead 4F, regardless of any RS-T deviation in this lead.

Contraindications to the test are an abnormal control electrocardiogram, congestive heart failure, or recent myocardial infarction (within the preceding four months). According to Levy,⁵ the test should not be repeated within 24 hours.

Of 300 consecutive patients tested by us, not one showed an abnormal anoxemia test when both the single and double "2-step" tests were normal. On the other hand, we have found the anoxemia test to be abnormal in only 20 to 30% of patients with definite coronary artery disease and abnormal "2-step" tests, though it has been reported to be abnormal in approximately 50% of patients with organic heart disease.⁷ The failure of the 10% oxygen test to be abnormal in the presence of coronary artery disease may be explained by the severity of the criteria as well as by the variability of the oxygen saturation of the blood during the procedure. Because of the latter, Malmström⁸ has introduced a modified hypoxia test, utilizing a mixture of 6.5% oxygen, 4.5% carbon dioxide, and 89% nitrogen.

The anoxemia test was performed in 38 of the 100 patients with abnormal "2-step" tests mentioned above. Ten anoxemia tests were abnormal in this group (26%), 23 were normal, and 5 were borderline. The frequency of a normal anoxemia test in the presence of definite coronary artery disease is illustrated by the following case.

S. I., a white man, 38, gave a one year history of severe, typical angina pectoris. Although the electrocardiogram at rest was normal, "2-step" tests were repeatedly abnormal, with an RS-T segment depression of as much as 3 to 4 mm. and marked T-wave inversions. Tracings taken during spontaneous anginal seizures disclosed similar alterations. The anoxemia test, however, was normal (fig. 5). Transient electrocardiographic alterations, recorded five minutes after breathing 10% oxygen, were insufficient to meet the necessary criteria, and later tracings were all normal. A second anoxemia test, done some time later, was also normal. A follow-up study of this patient revealed a "status anginosus," which was unrelieved by left cervicodorsal sympathectomy. On numerous occasions the patient has had prolonged attacks of acute coronary insufficiency, with characteristic electrocardiographic abnormalities.

It is accepted that normal anoxemia tests do not rule out the presence of organic heart disease. On the other hand, it is claimed that abnormal anoxemia tests are of definite diagnostic significance. However, the value of this procedure is limited not only by the relatively low percentage of abnormal results in patients with organic heart disease, but also by the definitely abnormal results in patients with neurocirculatory asthenia and anxiety states, despite the stringent criteria. Thus, of the 10 abnormal anoxemia tests in the group of 38 described above, 2 occurred with psychoneurotic patients with functional heart disturbance. One of these cases has been reported in detail previously.⁹

The danger of the 10% oxygen test also should not be minimized. Even when the tests are normal, circulatory collapse, shock, and convulsions may appear suddenly. The incidence of such reactions was 2% in our series of 300 cases. Usually the immediate administration of 100% oxygen results in prompt recovery. In cardiac patients, however, such reactions are serious, and death has occurred during the procedure.⁵

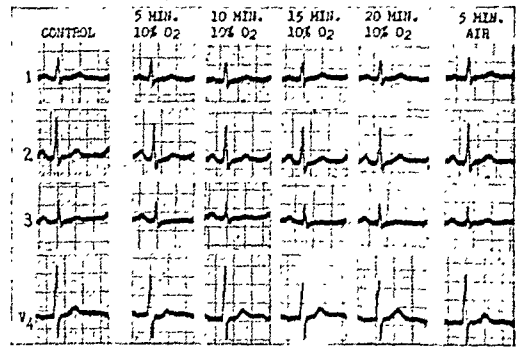


Fig. 5.—Anoxemia test of S. I., a 38 year old man with severe angina pectoris for one year. Control electrocardiogram is normal. Similar changes occurred with spontaneous anginal attacks as with abnormal "2-step" tests. Anoxemia (10% oxygen) test is normal.

In summary, the anoxemia (10% oxygen) test is not recommended as a routine cardiac function test in industry because of its relatively limited diagnostic value and inherent danger.

BALLISTOCARDIOGRAM

The ballistocardiograph became available as a practical cardiac function test apparatus in 1949 with the introduction of the direct body recording technique by Dock and Taubman.⁹ The instrument records the motion of the body induced by the contraction of the heart and the surge of blood into the arterial tree during each cardiac cycle. We have investigated the value of ballistocardiography in more than 600 patients during the past year, using a modified Dock type photo cell apparatus.¹⁰

6. Master, A. M.; Pordy, L., and Kolker, J.: Ergotamine Tartrate and "Two-Step" Exercise Electrocardiogram in Functional Cardiac Disturbance, *J. Mt. Sinai Hosp.* 15: 164, 1948.

7. Burchell, H. B.; Pruitt, R. D., and Barnes, A. R.: Stress and Electrocardiogram in Induced Hypoxemia Test for Coronary Insufficiency, *Am. Heart J.* 36: 373, 1948.

8. Malmström, G.: Cardiological Anoxemia Test with Special Reference to its Standardization; Clinical and Physiological Study, *Acta med. scandinav. supp.* 195: 1, 1947.

9. Dock, W., and Taubman, F.: Some Techniques for Recording the Ballistocardiogram Directly from the Body, *Am. J. Med.* 7: 751, 1949. Dock, W.; Mandelbaum, H., and Mandelbaum, R. A.: Ballistocardiography in Medical Practice, *J. A. M. A.* 146: 1284 (Aug. 4), 1951.

Method.—The patient lies prone on an immobile table. The longitudinal ballistic body motions are transmitted by a crossbar on the shins. This cuts the light falling on a photoelectric cell pick-up device. The record is taken on the customary electrocardiographic machine. We have devised a dual apparatus of the Dock body type, which permits the recording of either photocell (displacement) or electromagnetic (velocity) ballistocardiograms.¹¹ For time reference, simultaneous electrocardiograms and ballistocardiograms may be taken simply, even on single channel electrocardiographs. The ballistocardiogram is then recorded during quiet respiration and deep inspiration and expiration.

Criteria for Interpretation of Ballistocardiogram.—The normal ballistocardiogram, as illustrated in figure 6, is of a W-shaped appearance. According to Starr,¹² the component waves are labeled in alphabetical order, starting with the letter "H" (this represents the first headward motion occurring with each cardiac cycle). The

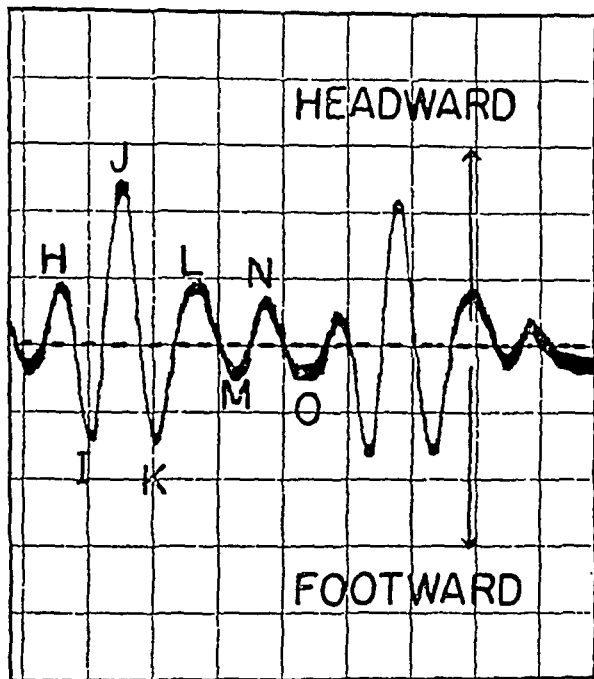


Fig. 6.—Normal ballistocardiogram. Key: H = apical thrust; I = ejection in early systole; J = impact on aortic arch and acceleration in aorta; K = deceleration in descending aorta; LMNO = after vibrations or forced thrusts.

key in the legend of figure 6 presents the cardiovascular events associated with the various waves. No attempt has been made, with this method, to interpret the ballistocardiographic tracings on a quantitative basis, as a measure of cardiac output. The records have been interpreted solely on the qualitative appearance of the component waves of the ballistocardiogram. The amplitude of the I-wave is normally slightly less than that of the K-wave. The J-wave is the most prominent headward wave.

10. Pordy, L., and others: Clinical Evaluation of the Ballistocardiogram. I. Normals, *Am. Heart J.* 42: 321, 1951. Chesky, K., and others: Clinical Evaluation of the Ballistocardiogram. II. Heart Disease—Hypertension, Angina Pectoris and Myocardial Infarction, *ibid.* 42: 328, 1951. Taymor, R. C., and others: The Ballistocardiogram in Coronary Artery Disease, *J. A. M. A.* 148: 419 (Feb. 9) 1952. Moser, M., and others: The Ballistocardiogram in Myocardial Infarction: Study of One Hundred Cases, *Circulation*, to be published.

11. Pordy, L., and others: The Dual Displacement and Velocity Ballistocardiograph Apparatus, to be published.

12. Starr, I.; Rawson, A. J.; Schroeder, H. A., and Joseph, N. R.: Studies on Estimation of Cardiac Output in Man and of Abnormalities in Cardiac Function, from Heart's Recoil and Blood's Impacts; Ballistocardiogram, *Am. J. Physiol.* 127: 1, 1939.

There is a normal respiratory variation in the amplitude of the complexes, i. e., the waves are of greater amplitude during inspiration than during expiration. Abnormal ballistocardiogram patterns include: (1) diminished or absent I-waves; (2) exaggeration of the normal respiratory variation, i. e., the amplitude of waves during expiration are 50% or less than that during inspiration; (3) definitely slurred or notched I, J, or K-waves; (4) prominent H-waves (early M-pattern); (5) late, deeply notched J-waves (late M-pattern); (6) prominent diastolic waves (L, M, N, etc.); (7) deep, wide, or absent K-waves; (8) low amplitude or totally bizarre complexes. These alterations may occur alone or in various combinations in any one case.

Results.—The ballistocardiogram at rest is normal in approximately 90% of normal patients. Our criteria for the selection of normal persons in this study included a normal double "2-step" exercise electrocardiogram as well as normal routine cardiac findings. An abnormal ballistocardiogram is of greater diagnostic value in patients under 50 because thereafter the tracing may be altered by the normal physiological aging processes. Normal ballistocardiogram records in patients over 50, however, are of definite diagnostic significance.

The ballistocardiogram is of value in the diagnosis of coronary artery disease. In 93% of patients with angina pectoris who had abnormal resting electrocardiograms, the ballistocardiograms were also abnormal. In 85% of patients with angina pectoris who showed normal resting electrocardiograms but abnormal "2-step" exercise tests, the ballistocardiograms even at rest were abnormal. This figure increased to 90% after standard exercise. Since cardiac ejection may be altered only after exertion the ballistocardiogram should be recorded after standard exercise if the resting record is normal. We found a close correlation between abnormal "2-step" exercise tests and abnormal ballistocardiograms. Because one records electrical and the other mechanical events, both should be employed routinely in the evaluation of cardiac function.

The ballistocardiogram is abnormal in an extremely high percentage of hypertensive patients; in such cases, therefore, the cardiac diagnostic value of the procedure is limited. After lowering of the blood pressure by sympatholytic drugs, we have, indeed, observed the ballistocardiogram revert to normal. Eighty-one per cent of patients with previous myocardial infarction showed abnormal ballistocardiograms at rest, whether the resting electrocardiogram was abnormal or not.

The ballistocardiogram has been reported to be of great help in the management of patients with acute rheumatic fever and other acute diseases of the heart, as well as of those with myocardial infarction. By its use corroborative diagnostic evidence may be obtained in cases of coarctation of the aorta.

To the simplicity of the technique of recording the Dock type ballistocardiogram is added the advantage of the absence of danger to the patient. This is of obvious importance in industrial medicine. The ballistocardiogram reflects the functional state of the heart, regardless of the type of cardiac pathological condition present. Therefore, ballistocardiography appears to be a safe and valuable instrument supplementary to electrocardiography for the routine study of cardiac function.

KRASNO-IVY NITROGLYCERIN FLICKER TEST

In 1950 Krasno and Ivy¹³ described a reliable, portable machine, the "flicker photometer," or "flicker meter," for cardiac diagnosis in office practice. The "flicker photometer" is used to determine the threshold of the fusion frequency of flicker (FFT). The fusion frequency of flicker is that frequency at which successive flashes of light appear continuous, or free from flicker, to the patient. The machine is so constructed that one may easily regulate the number of flashes of light delivered per minute.

Method.—The patient is seated comfortably in a quiet room, 5 ft. from the frosted glass window of the machine. Tobacco, alcohol, and vasodilator drugs should not be taken prior to the test. If glasses are worn ordinarily, they should be used during the examination. The light source of the room must be directed away from the patient's eyes.

After a 10 minute rest, the test is started, and the machine is turned on. The patient is instructed to say "now" when the light in the frosted glass window first appears to flicker, while the operator controls the flicker rate knob. Three successive similar readings serve as the control fusion frequency of flicker, or baseline for the subject. After sublingual administration of nitroglycerin (1/150 grain), the procedure is repeated at two minute intervals for six minutes. This constitutes the single test. If any one of the postnitroglycerin administration baselines or fusion frequency of flicker does not vary from the control by ± 60 flashes per minute, "no change" has occurred ("fixed" response). The procedure is then repeated after a second nitroglycerin tablet has been given (the double test). Intravenous or intramuscular papaverine (50 mg.) may be substituted for the nitroglycerin.

Criteria for Interpretation.—A normal response is one in which the fusion frequency of flicker after nitroglycerin administration is decreased by 60 flashes or more per minute below the patient's baseline. Abnormal tests are those in which the fusion frequency of flicker readings after nitroglycerin administration are increased by 60 flashes or more per minute above the patient's baseline.

The impairment of the fusion frequency of flicker after nitroglycerin administration in normal persons is explained by vasodilatation, with resultant passive congestion of the retina. Krasno and Ivy noted an "abnormal" response in 99% of patients with hypertension or coronary artery disease. The improvement of the fusion frequency of flicker after nitroglycerin administration in such cases is said to be related to the relief of vasospasm and the resultant active hyperemia of the retina. The nitroglycerin flicker test is described as an aid in the diagnosis of equivocal cases of coronary artery disease and hypertension.

Results.—We have studied the nitroglycerin flicker test with Dr. Jack Matis, of New York, in a preliminary group of 126 patients. There were 83 men and 43 women, whose ages ranged from 17 to 83 years. Thirteen of those tested were normal. They were selected on the basis of normal cardiac findings, including a normal resting electrocardiogram and, in most instances, a normal double "2-step" test. In this normal group the nitroglycerin flicker test showed a normal response in eight and an

abnormal one in five. In one patient with diabetes mellitus and no clinical evidence of heart disease, the Krasno-Ivy test was abnormal. The remaining 112 patients all showed definite evidence of organic heart disease, on either a hypertensive or arteriosclerotic basis in most instances. The nitroglycerin flicker test in the cardiac group was abnormal in 85 patients, gave a "fixed" response in 14, and was normal in 13.

The results of the nitroglycerin flicker test will be correlated with the results of other cardiac function tests, and the findings reported later. Our preliminary work does not, as yet, permit a final evaluation of this test. It may be stated that the test has the disadvantage of depending on a subjective response of the patient. This may be overcome, however, by careful technique on the part of the examiner. A second objection to the procedure lies in the assumption that retinal vasospasm is indicative of coronary arterial spasm. Since the test is relatively easy to perform and without patent danger, however, its further study, in relation to the older, more established procedures, is recommended.

The discussion has been limited to the four procedures described. The value of circulation time, venous pressure, vital capacity readings, and roentgenokymograms in the study of cardiac function has been accepted for years, and, therefore, these tests have not received special consideration in this paper. Newer promising methods, such as the oxygen consumption during exercise,¹⁴ may prove to be practical for measuring cardiac reserve. The importance of standardization of procedures in cardiac diagnosis cannot be overemphasized.

SUMMARY AND CONCLUSION

The necessity for dependable cardiac function tests, especially in industry, is demonstrated by the large number of patients with heart disease in whom the routine clinical studies are all normal. The "2-step" exercise electrocardiogram test is described. Its value is confirmed by follow-up studies of 200 patients with normal and abnormal tests. A diagnosis of coronary insufficiency is practically, but not absolutely, excluded if both the single and double "2-step" tests are normal. An abnormal single or double "2-step" test is objective evidence of coronary insufficiency. The anoxemia (10% oxygen) test is not recommended for the routine evaluation of cardiac function in industry. Its yield of abnormal tests in cardiac patients is relatively small. It is hazardous and requires constant supervision. Ballistocardiography, by the simple Dock technique, is described as a valuable supplement to electrocardiography and exercise tests in the cardiac diagnostic armamentarium. It is too early to evaluate properly the Krasno-Ivy nitroglycerin flicker test, but further study of it is definitely warranted.

In industry, as in clinical practice, a battery of cardiac function tests should be employed routinely and regularly for the early detection of pathological cardiac states and for the accurate evaluation of heart function.

1150 Park Ave. (Dr. Pordy).

13. Krasno, L. R., and Ivy, A. C.: Response of Flicker Fusion Threshold to Nitroglycerin and Its Potential Value in Diagnosis, Prognosis and Therapy of Subclinical and Clinical Cardiovascular Disease, *Circulation* 1: 1267, 1950.

14. Chesky, K., and Sise, H. S.: Use of Oxygen Consumption During Exercise as a Quantitative Measure of Cardiac Reserve, abstracted in *Proc. Am. Fed. Clin. Research* 5: 20, 1949.

CATION EXCHANGE RESINS AS AN ADJUNCT IN TREATMENT OF HEART FAILURE

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Restriction of sodium in the diet has been accepted as helpful in the management of many patients with congestive heart failure and certain patients with other forms of edema, but the ideal sodium intake cannot always be accomplished by diet alone. In 1946, Dock¹ suggested that a cation resin could be used to remove sodium, potassium, calcium, and magnesium from ingested foods and further indicated that such a resin was nontoxic for dogs and rats. Extensive studies in animals² have demonstrated further the absence of toxicity from cation resins over short and long periods. These observers find that prolonged administration of the ammonium form of resin has not interfered with health, nutrition, or hematological development of animals. A detailed review³ of the literature on ion exchange resins and edema discusses fully the rationale for the use of these substances.

A cation exchange resin can also restrict the absorption of sodium from the human intestine,⁴ and its use has been found practical and effective in man.^{4b, d} The availability of a large number of sodium ions in solution in the gut and a relatively low concentration in solution of certain other cations^{4a} favors fixation of large amounts of sodium over calcium and magnesium, for example. However, the problem of potassium fixation and interference with potassium absorption initially offered some difficulty. Early experience with the ammonium form of a cation exchanger indicated consid-

erable loss of potassium as well as sodium via the stools, so that doubt was expressed as to the advisability of administration of this form of resin to patients for fear of hypokalemia.^{4b, d, f}

The solution to this problem has been brought to our attention on a previous occasion.^{4b, c, d} A mixture of ammonium and potassium forms a carboxyl resin leads to the formation of potassium chloride and ammonium chloride in the acid pH of the stomach. As these substances enter the upper intestine both ammonium chloride and potassium chloride are absorbed before the rising pH of the intestine activates the resin and fixes the cations of NH_4^+ and K^+ , as well as Na^+ and other cations. In this fashion, enough extra K^+ is absorbed to offset the K^+ fixed in the gut by the resin. Also, ammonium chloride is absorbed in considerable amount.

In a previous communication,^{4b} we have shown through a study of urinary secretion of potassium and serum potassium levels that the above hypothesis appears to hold in man and that certain cation exchange resins may be used with reasonable safety in the management of edema. It is the purpose of this discussion to outline the use of a cation exchange resin (resodec®)⁵ in the treatment of congestive heart failure and certain other forms of edema. Our original experience with 10 patients^{4b} has been expanded to a total of 50, of whom 35 are discussed here. Resodec® has been administered to three subjects without edema, 22 patients with congestive heart failure, 5 with cirrhosis of the liver and ascites, 3 with the edema of the nephrotic syndrome, and 2 with constrictive pericarditis and edema. Studies including 24-hour urine excretion of sodium and potassium, interval determinations of plasma chloride, plasma bicarbonate, serum sodium, serum potassium, and blood urea have been carried out in many hospital patients, while less detailed study has been made in a few outpatients. Frequent weight recordings have indicated gain or loss of edema.

INDICATIONS

The cation resin is not a cure-all and not a complete solution to the sodium restriction problem in patients with edema. A subsequent paragraph will indicate that the capacity of the resin is not sufficient to restrict sodium absorption from a full diet, and a patient must not expect to eat as much salt as he wishes. Furthermore, the cation resin is not indicated in all patients with heart failure. Many patients with congestive heart failure respond to rest, digitalis, and moderate dietary restriction of sodium and will remain compensated for months or even years under such a regimen. However, other patients with heart failure and edema are unable to attain a suitable level of sodium restriction. In these, proper administra-

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1. Dock, W.: Sodium Depletion as a Therapeutic Procedure: The Value of Ion-Exchange Resins in Withdrawing Sodium from the Body, *Tr. A. Am. Physicians* 59: 282, 1946.

2. Flanagan, T. L.; Sax, M. F., and Heming, A. E.: Toxicity Studies on Amberlite XE-96, a Carboxylic Type Cation Exchange Resin, *Federation Proc.* 10: 295 (March) 1951.

3. McChesney, E. W.; Dock, W., and Tainter, M. L.: Ion Exchange Resins in Edema, *Medicine* 30: 183 (May) 1951.

4. (a) Irwin, L.; Berger, E. Y.; Rosenberg, B., and Jackenthal, R.: The Effect of a Cation Exchange Resin on Electrolyte Balance and Its Use in Edematous States, *J. Clin. Invest.* 28: 1403 (Nov.) 1949. (b) Hay, S. H., and Wood, J. E., Jr.: Cation Exchange Resins in the Treatment of Congestive Heart Failure, *Ann. Int. Med.* 33: 1139 (Nov.) 1950. (c) Heming, A. E., and Nance, J. W.: Personal communication to the authors. (d) Kahn, S. S., and Emerson, K., Jr.: Experiences with the Use of Cation Exchange Resins in the Treatment of Edema, *J. Clin. Invest.* 29: 827 (June) 1950. (e) Danowski, T. S.; Greenman, L.; Mateer, F.; Peters, J. H.; Weigand, F. A.; Mermelstein, H., and Clark, C. E.: Carboxylic Cation Exchange Resin Studies in Animals and Humans, *ibid.* 29: 807 (June) 1950. (f) Kraus, H.: The Use of a Cation Exchange Resin in Patients with Cardiac Edema, *ibid.* 29: 829 (June) 1950. (g) Currens, J. H.; Counihan, T., and Rourke, M.: Observations on the Administration of Ammonium Cation Exchange Resin to Patients with Cardiac Edema, *ibid.* 29: 807 (June) 1950.

5. Resodec® used in the study has been furnished by Smith, Kline and French of Philadelphia. It is a highly cross-linked, polyacrylic polycarboxylic cation exchange resin. It contains enough of the potassium resin to provide 20 mEq. of potassium per dose, and the balance is made up of ammonium resin. This figures out to 3.33 gm. (dry weight) of potassium resin and 11.67 gm. (dry weight) of ammonium resin.^{4c} This is referred to in this paper as resin 3.

tion of a cation resin may be helpful as an adjunct in treatment. This is particularly true of patients with long-standing chronic congestion who have become refractory to mercury. In brief, the more severe and more refractory cases of congestive heart failure appear to be the ones to whom this principle may be properly applied.

In addition, as noted below, it has been our experience that the obstinate edema associated with nephrosis may sometimes respond to this method of therapy. Diuresis in several patients with cirrhosis of the liver and ascites has followed resin administration alone, while potentiation of mercurial diuresis by the cation resin has been particularly striking in patients with cirrhosis. Recently, an excessive edematous patient with constrictive pericarditis was better fitted to face the ordeal of operation after the use of a cation resin.

DOSAGE AND ADMINISTRATION

The dosage of resodec® and the diet to be recommended during its administration depend somewhat on the degree and duration of the edema and the patient's initial reaction to resin administration. The resin appears to work at full capacity in the normal person who does not have edema.^{4c} Our own experience is shown in figure 1. Here a decrease in urinary sodium excretion is very marked with the feeding of resodec® to a normal subject for three days. Continued depression of urinary sodium excretion for at least two days after discontinuance of the resin has been commonly observed. In the patient with congestive heart failure, however, the amount of sodium bound by the resin appears to be somewhat lower, the reason for this remaining unclear at the moment.^{4c} It has been our experience^{4b} that the ammonium cation resin is somewhat more efficient gram for gram as regards the binding of the sodium than the ammonium-potassium resin, but the disparity has not been great, and in nearly all patients receiving the ammonium-potassium resin we have found the dosage of 15 gm. three times daily to be adequate when the patient was on a 1,000 mg. intake of dietary sodium (2.5 gm. of salt). Only an occasional patient has profited by larger dosage of cation resin, and more than a total of 60 gm. daily is unnecessary with this diet. A few instances of severe congestive heart failure have required still further dietary restriction to 500 mg. of dietary sodium daily (1.25 gm. of salt), but we have kept the resin dosage at 15 gm. three or four times daily. A bedtime dose of 15 gm. of resin has not proved salutary in our experience. When larger dosage is required, it should be given after the regular meals rather than at bedtime. It would appear that sufficient experience has accumulated⁶ to indicate that the ammonium potassium cation carboxylic resin has an adequate capacity for therapeutic purposes and may prevent, in dosage of 45 to 60 gm. daily, the absorption of 40 to 100 mEq. of sodium. This, as indicated, will vary with the individual patient, depending chiefly on the degree of his edema and the magnitude of his sodium intake. After various trials, it appears wiser to us to administer the cation resin intermittently, four days on and three days off. In this study and previously^{4b} it has been noted that sodium absorption restriction has continued one to five days after the resin dosage has been discontinued, the lag averaging about three days. Many

patients appreciate the three days without resin and appear to get along somewhat better on this schedule.

For certain other patients who have been dependent on regular injections of mercury prior to the use of resin, it has been found that, once they can be brought out of the edematous state, it may be possible to maintain them edema-free on a slightly smaller dose of resin, namely, 15 gm. twice daily.

The taste of the resin is not pleasant, and it is best to take it in fruit juice, preferably one-half glass of grapefruit juice, stirred or shaken well and swallowed immediately. Although a few patients object strenuously to the taste, we have not found this to be a serious handicap, and those sick enough to require the resin generally overlook this relatively minor inconvenience.

GENERAL AND SPECIFIC EFFECTS

Some effects produced by administration of an ammonium and potassium resin (resodec®) have been observed in the study of 35 patients. It is not always

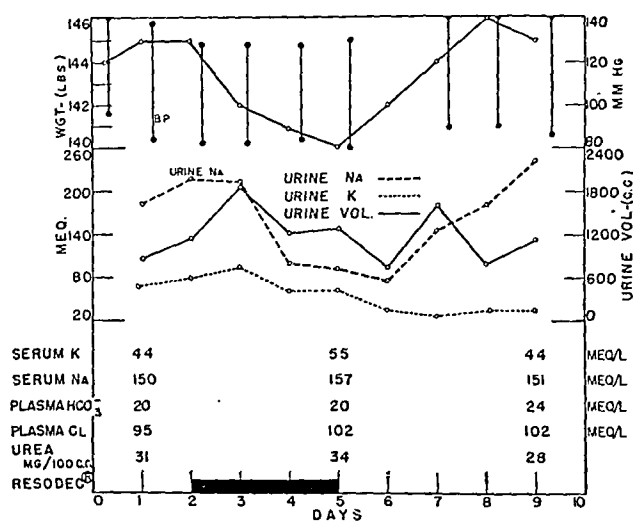


Fig. 1.—W. M., 54. Effect of ammonium cation resin, 45 gm. daily, on a subject with no disease and on a normal diet.

possible to explain all of these or to evaluate the true therapeutic value of the cation resin while other measures of treatment are being used. However, it was our impression that the resin produced a decided restriction of sodium reabsorption in the three nonedematous patients studied, perhaps a mild acidosis and perhaps a slight elevation of plasma chloride (fig. 1). In this and other^{4b} studies on normal subjects, restricted sodium absorption was demonstrated by a sharp decline in urinary sodium excretion during resin administration and, as noted above, the effect lasted several days after the resin was discontinued.

In cardiovascular patients with edema, 15 of 22 patients showed additional clinical improvement, which seemed to be attributable to the resin. In seven of these the results were striking, as conventional measures with digitalis, ammonium chloride, and mercury had previously failed.

6. Irvin, Berger and Rosenberg,^{4a} Hay and Wood,^{4b} Kahn and Emerson,^{4c} Dock, W., and Frank, N. R.: Cation Exchangers: Their Use and Hazards as Aids in Managing Edema, *Am. Heart J.* 40: 638 (Oct.) 1950.

The salutary effect of restriction of sodium absorption is well illustrated in H. E. (see accompanying table). This patient, a woman of 60, with advanced rheumatic heart disease, aortic regurgitation, and mitral stenosis, had had congestive heart failure and edema for months. For over a year she had received a mercurial diuretic every 10 days, each injection preceded for three days by 6 to 8 gm. of ammonium chloride daily. This routine became less and less effective, and she entered the hospital for ammonium potassium cation resin therapy (Day 1, table). Up to this time she had been on a diet of 1,000 mg. of sodium, to which she had faithfully adhered. Complete digitalization with digitoxin had been maintained for years and the daily ration unchanged. No medication was given except the usual digitoxin and resodect.[®] Although excreting no urinary sodium at the time, owing to progressive fluid retention, her urinary sodium remained at zero after resodect[®] therapy in spite of steady diuresis and loss of edema. Urinary potassium excretion was maintained at adequate levels, and serum potassium remained normal. Plasma chloride levels remained normal in spite of marked diuresis, and a mild to moderate

patients resodect[®] appeared to restore successful mercury diuresis where ammonium chloride had previously failed. The potentiation of mercurial diuresis by a cation resin has been noted by other observers. The mechanism involved is hard to clarify, as studies along this line are difficult to control. The obvious explanation, of course, would be the fact that a daily dose of 45 to 60 gm. of resodect[®] would be theoretically equivalent to a daily dose of approximately 8 to 10 gm. of ammonium chloride. Since this figure is slightly above the customary dosage of 6 to 8 gm. of ammonium chloride daily, it is entirely possible that the success of this cation resin in the potentiation of mercury may be due to a larger ammonium chloride dosage. However, the obvious advantage of potentiation of a mercurial diuretic plus the restriction of sodium absorption is well illustrated in figure 2. Here the postdiuresis reaccumulation of edema is avoided by sodium absorption restriction, and relief from heart failure proceeds smoothly and steadily. D. D. M., the patient for whom data is charted in figure 2, was admitted with rheumatic heart disease, mitral stenosis, auricular fibrillation and advanced congestive heart failure, marked

Results of Restriction of Sodium Absorption in Patient H. E.

Day	Weight, Lb.	Urine Ce./24 Hr.	mEq./24 Hr. Urinary		Serum Na	mEq./L.		Plasma HCO ₃	Mg. % Urea	Gm./Day Resin 3
			Na	K		Serum K	Plasma Cl			
1.....	137		..	..	...	...	...	..	..	..
2.....	136¼	2,120	0	33	...	...	102	24	36	..
3.....	135¾	4,500	0	63	...	...	...	..	..	60
4.....	133¼	3,070	0	47	144	4.6	...	..	..	60
5.....	130½	3,170	0	65	...	...	...	..	..	60
6.....	128¾		..	..	...	...	104	13	..	45
7.....	128½		..	..	...	...	...	..	..	45
8.....	127½	2,370	0	20	...	...	...	..	..	45
9.....	124½		..	..	145	4.1	104	15	37	45
10.....	124		..	..	...	...	...	..	..	45
11.....	124	2,950	0	30	...	...	...	..	..	45
12.....	122¼		..	..	150	4.8	104	18	25	30
13.....	121		..	..	...	...	...	..	..	30
14.....			..	..	...	...	...	..	..	..
24.....	124	2,600	0	33	...	...	...	..	..	30
25.....	124		..	..	141	4.4	95	20	32	30
60.....	123		..	..	...	...	107	21	38	30

loss of plasma bicarbonate returned toward normal even with continued resin administration. The patient was discharged on the fifth hospital day and handled thereafter as an outpatient. On the 12th day resodect[®] was reduced to 30 gm. daily and relatively edema-free weight maintained on this dosage. No diuretic of any kind has been given since the first day of resodect[®] therapy, and she has continued to remain up and around with minimal edema on this regimen for over two months.

In 16 of these 22 patients with congestive heart failure, slight to moderate diuresis occurred with the resin alone, and in two patients a marked diuresis occurred with the resin alone.

The mechanism by which a cation resin produces diuresis is not clear, unless it be the ammonium chloride effect as well as the restriction of sodium absorption. In 8 of 18 cases, marked potentiation of the mercurial diuretic followed the administration of resin and moderate potentiation of the mercurial diuretic followed resin administration in 3 cases, with a slight or indifferent effect in 7. The remaining four patients with congestive heart failure did not require a mercury diuretic. In five

edema and ascites. Heart failure had occurred four and one-half months before, while edema and ascites had increased in spite of rest in bed, digitalization, and dietary salt restriction. Repeated mercurial injections had become progressively ineffective. Diuresis and loss of edema began with resin alone, and marked potentiation of mercury reappeared. Progressive loss of edema proceeded with a zero urinary excretion of sodium, but a continued urinary potassium excretion and adequate serum potassium levels. Early intermittent resodect[®] dosage gave way to smaller (15 gm. twice daily) dosage, with absence of edema despite resumption of activity. Plasma chloride levels were well maintained except after marked mercurial diuresis on the 20th day, but resumption of resodect[®] therapy was followed by normal plasma chloride levels.

The whole question of potentiation of mercurial diuretic by a cation resin needs further study. In this regard it may be noted that resodect[®] brought about an elevation of the plasma chloride from a lower to a higher figure in 15 of 16 patients with congestive heart failure where this observation was made. Furthermore, a mild

to moderate acidosis was produced in 10 of 14 patients with congestive heart failure. Cation resin administration, therefore, leads to the two states commonly accepted as necessary for potentiation of mercurial diuresis, namely, adequate plasma chloride levels and diminished plasma bicarbonate levels.⁷ Again it is not clear whether these two effects are the result of ammonium chloride absorption associated with administration of ammonium-potassium cation resin or a combination of this and the restriction of sodium absorption.

CONTRAINDICATIONS, DANGERS, AND DISCOMFORTS

With the ammonium potassium form of the cation resin (resodec[®]) relatively little gastrointestinal irritation has occurred. In 4 of the 35 patients some nausea and vomiting followed the ingestion of the resin; two of these were in the nephrosis group. One of the patients with nephrosis, however, was able to overcome this difficulty, and definite fluid loss followed. Rectal irritation with a slight burning sensation of the rectum was a common complaint, but this was minor in all instances. We have not encountered fecal impaction in the moderate dosage recommended in this communication. Diarrhea occasionally sets in but may disappear with curtailed dosage. It is our impression that the unfavorable gastrointestinal effects previously reported may have been due to larger dosage. Taste of the ammonium-potassium cation resin resodec,[®] as noted above, though not pleasant is certainly not prohibitive.

Depletion of potassium has not been a troublesome feature with the use of the ammonium-potassium form of the resin. The lowest serum potassium level noted fell within the range of normal, namely, 3.2 mEq. per liter. Normal serum potassium levels, of course, are not proof against potassium depletion, but continued positive urinary potassium excretion offers added evidence that adequate potassium was available to the patient. Clinical evidence of hypokalemia has been suggested in only two patients, in whom digitalis toxicity, unexplained by edema loss alone, seemed to develop.^{4b} Balance experiments must finally settle this matter, but, in the absence of clinical signs or symptoms and with liberal daily potassium excretion in 26 treated patients studied, it would seem unlikely that hypokalemia could be a hazard with an ammonium-potassium cation resin. Contrariwise, we have had no instances of potassium poisoning, although care has been taken to avoid the prolonged administration of cation resin to patients with renal insufficiency.

We have not studied calcium and magnesium metabolism in these patients, but a previous balance study^{4a} indicates that no detectable calcium deficiency occurs.

Acidosis would appear to be only a moderate hazard. We were able to study this feature in 23 of our 35 patients. Fifteen of these patients had a carbon dioxide-combining power below 20 mEq. per liter, the lowest being 11 mEq. per liter. On a number of occasions we have seen the plasma bicarbonate fall slightly to moderately, only to recover to more normal levels with a continuation of resin (see accompanying table). This sequence is based on the increased ammonium production by the kidney and is similar to events following ammonium chloride administration.^{4a,d} In no instance has

the acidosis appeared to be a clinical hazard where adequate renal function was present, and its value in the potentiation of mercury diuresis has been alluded to above. So far we have worked with only the ammonium, hydrogen, and ammonium-potassium exchangers, and we are unable to comment at length at this time on the possible value of the mixture of an anion resin with an ammonium-potassium resin to offset acidosis.⁸ It is our impression that reaction of plasma bicarbonate levels following this mixture is somewhat similar to the effects produced by other resins.

LOW SALT SYNDROME AND RENAL INSUFFICIENCY

The hazard of the low salt syndrome has been set aside for separate discussion, owing to its obvious importance. The continued use of a potent cation resin in patients similar to the ones described here might well lead in some to the dangerous low salt syndrome already adequately described by Schroeder several years ago.⁹ This occurred in our study twice. In one, during resin

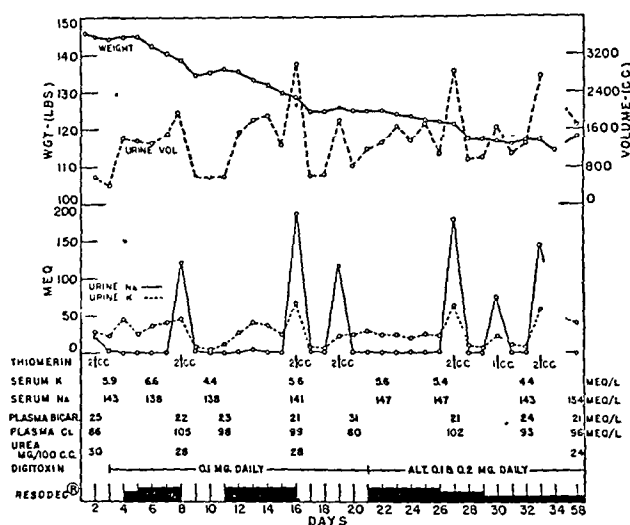


Fig. 2.—D. D. M., 25, married, female. Severe congestive heart failure with ascites and edema. Highest black rectangle represents 60 gm. of resin daily, next lowest 45 gm. daily, and final maintenance dosage of 30 gm. daily. Patient received approximately 1,000 mg. of dietary sodium daily.

therapy, the serum sodium was 139 mEq. per liter, with a low plasma chloride of 86 mEq. and a serum potassium of 3.6 mEq. per liter. The blood urea rose, and the patient appeared to be quite sick but responded to hypertonic salt intravenously and potassium chloride by mouth with subsequent diuresis, restoration of normal blood urea levels, and a return of appetite. It is our impression from this and other experiences that it is inadvisable to administer the cation resin to patients who are not eating well, and it cannot be emphasized too strongly that the

7. Ethridge, C. B.; Myers, D. W., and Fulton, M. N.: Modifying Effect of Various Inorganic Salts on the Diuretic Action of Salyrgan. *Arch. Int. Med.* 57: 714 (April) 1936. Evans, W. A., Jr.: The Effect of Salt and Water Metabolism Upon Salyrgan Diuresis (with Special Reference to the Effect of Permanent Bile Fistula), in *Medical Papers Dedicated to Henry Asbury Christian*, Boston, R. T. Monroe, 721 Huntington Ave., 1936, p. 204-222.

8. Martz, B. L.; Kohlstaedt, K. G., and Helmer, O. M.: The Use of Ion Exchange Resins in the Management of Congestive Heart Failure and Cirrhosis of the Liver, *J. Lab. & Clin. Med.* 36: 962 (Dec.) 1950.

9. Schroeder, H. A.: Renal Failure Associated with Low Extracellular Sodium Chloride: Low Salt Syndrome, *J. A. M. A.* 141: 117 (Sept. 10) 1949.

use of a cation resin in the face of renal insufficiency is probably an extremely dangerous and hazardous procedure.

In one patient with chronic glomerular nephritis, uremia, and massive edema, the resin was deliberately used in the face of renal insufficiency, with resulting moderately severe acidosis. Considerable edema fluid was lost, with relief to the patient, but the blood urea mounted rapidly from 88 mg. per 100 cc. to 177 mg. per 100 cc. Renal insufficiency has been commonly accepted as a prime contraindication to cation resin administration. Effects of sodium depletion by resin therapy during uremia and the unfavorable mechanisms involved have been recorded recently.¹⁰

Emphasis must be placed on two dangers from cation resin administration: (a) possible production of the low salt syndrome and (b) aggravation of an already established renal insufficiency.

OTHER FORMS OF EDEMA

Five patients with cirrhosis of the liver, edema, and ascites have received the resin from 4 to 15 days. Four of the five patients studied had proved biopsy diagnosis of portal cirrhosis. Two patients showed a marked diuresis on resin therapy alone. The remaining three showed a marked mercurial effect following resin therapy, although mercury and ammonium chloride had previously failed in two.

Three patients with the nephrotic syndrome of chronic nephritis were studied. One appeared to be a failure largely because of the accompanying glomerulonephritis; obviously he was not a suitable candidate for the cation resin, which produced nausea. In the other who had the nephrotic syndrome associated with chronic glomerulonephritis, the renal function was good at the time, and a moderate diuretic response followed the cation resin alone. Also marked mercurial diuresis helped bring about a loss of 42 lb. (19 kg.) in a period of 23 days. Here again the diuresis may have been spontaneous and coincident with resin administration, but at least the patient had been refractory to the usual methods of treatment for six weeks prior to resin administration. This patient has remained well and edema-free for several months, with complete resumption of all activity. A less favorable experience occurred in a child of 6 years. For months she had been water-logged and refractory to treatment. Either coincident with or as a result of resin administration, moderate to marked diuresis occurred without and with mercury. Renal failure increased and azotemia mounted, so that the resin was discontinued. Again it would seem that adequate renal function in the nephrotic syndrome should be prerequisite to cation resin administration.

Two patients with constrictive pericarditis were observed after resin administration. One appeared to show a moderate loss of edema from resin effect, while the other benefited decidedly by moderate diuresis from the resin alone and moderate to marked potentiation of a mercurial diuretic.

MINIMAL PRECAUTIONS

The question has arisen on a number of occasions as to just what simple rules should be followed to insure relative safety during administration of a cation resin.

Obviously, all physicians may not be able to follow patients with detailed chemical analyses.

It would seem unwise to administer resin to a patient with an appreciable degree of renal insufficiency, and, generally speaking, nitrogen retention in the blood should be considered a contraindication to its use. Daily weight recordings are essential to the management of an edematous patient. Finally, a reasonably good appetite and a reasonably good flow of urine should be present before a cation resin is administered. During the early course of cation resin administration, there should be a slight to moderate increase in urinary flow. Moderate to marked diuresis nearly always follows a mercurial diuretic, and failure of mercurial diuresis during the course of resin administration may well be indicative of renal failure or the low salt syndrome or both. Hyperpnea, nausea, and vomiting are signals for immediate discontinuance of the resin, and these symptoms should be followed up by determinations of plasma chlorides, plasma bicarbonate, and blood urea, or similar blood nitrogen studies.

SUMMARY AND CONCLUSIONS

Resodec® has been administered to 50 subjects with and without edema for long and short periods. No serious uncontrollable toxic effects were noted. Some observations on 35 of these have been discussed. Hypokalemic effects encountered originally after the administration of an ammonium cation resin do not appear to occur with the ammonium-potassium cation resin. The low salt syndrome, azotemia, and mild to moderate transient acidosis represent the chief hazards associated with ammonium-potassium cation resin administration. Impaired renal function is the outstanding contraindication to its use. Restriction of sodium absorption is a useful therapeutic adjunct in certain patients with obstinate edema of heart failure, cirrhosis of the liver with ascites and edema, and perhaps edema of the nephrotic syndrome.

10. Nickel, J. F.; Lowrance, P., and Leifer, E.: Effect of Sodium Depletion and Repletion on Renal Function and Body Fluids During Uremia, abstracted, *J. Clin. Invest.* 30: 664 (June) 1951.

Cardiac Resuscitation.—In the treatment of cardiac arrest under anesthesia, it is essential to obtain an adequately oxygenated cerebral circulation. Time is vital. To do this, artificial respiration must be started at once. Simultaneously, the heart must be made to function as a pump by means of cardiac massage. Intracardiac injections with epinephrine or any other drug are useless because it is unlikely that the heart will resume beating effectively, but will merely fibrillate and consume further valuable oxygen and time. Moreover, from the point of view of ultimate recovery, the heart which is in ventricular fibrillation is more difficult to start than one which has completely stopped. Experimentally, it can be shown that cardiac massage in the presence of ventricular fibrillation produces a very poor output and under these conditions it is impossible to restore normal rhythm. If, on cardiac massage, the heart is found to be in fibrillatory state, every effort must be made to overcome it. Electrical defibrillators have been described for this purpose but they are not always readily available. In dogs, the application of ice to the fibrillating heart will inhibit it and enable normal rhythm to be started. This is, of course, applicable in man only when the thorax is open. An alternative method of stopping ventricular fibrillation is to supply the myocardium with oxygen. This can be done by intra-arterial transfusion with oxygenated blood sufficient pressure to force it back into the coronary circulation.—B. G. B. Lucas, *Some Observations on Anoxia, Anesthesia, and Resuscitation*, November, 1951.

TREATMENT OF SOME COMPLICATIONS OF COLLES' FRACTURE

Miland E. Knapp, M.D., Minneapolis

Colles' fracture is a fracture of the lower end of the radius, within 1 in. (2.54 cm.) of the articular surface of the radius, which may or may not be accompanied by a fracture of the styloid process of the ulna. The usual deformity is threefold: posterior displacement, posterior angulation, and radial deviation of the hand at the wrist. The bone ends are usually impacted. The injury results from a fall on the outstretched hand, and this accounts for the type of deformity produced.

In reducing the fracture, it is extremely important that the posterior displacement and angulation be corrected, so that there will be a full range of motion in volar flexion. The fracture is usually immobilized with the wrist in marked volar flexion, in order to obtain reduction of these deformities. It is frequently necessary that this be done, but in the majority of cases, immobilization may be carried out with the wrist straight or in slight flexion. Since exaggerated volar flexion is a position in which normal function is almost impossible, it is important that the wrist be placed in as nearly a straight line as is consistent with maintenance of the reduction. The wrist should be replaced in a functional position as soon as possible; usually, this can be done within two weeks after the injury. It is equally important to restore ulnar deviation, so that radial deformity of the wrist will be avoided. If impaction is severe, the fracture cannot be reduced until disimpaction has been performed. Disimpaction should be done as gently as possible, but, even with the greatest care, it may leave the lower end of the radius with a bony deficiency that requires prolonged immobilization in ulnar deviation to enable healing without deformity. Since ulnar deviation is a position of function, maintenance of this position, even for six to eight weeks, does not endanger function of the hand, if the fingers are used for ordinary purposes during the period of fixation.

Colles' fracture is probably the commonest of all fractures. It is treated by general practitioners, interns, residents, general surgeons, and orthopedists. Its frequency renders it less formidable to the medical profession. The majority of cases result in painless function and a satisfactory range of motion after enough time has elapsed; however, bad end results and prolonged disability not infrequently follow Colles' fracture. This is rarely the result of inadequate reduction, since every clinical teacher emphasizes the necessity for adequate reduction in all fractures. The poor results are usually a consequence of lack of recognition of the importance of soft tissue damage as a cause of disability following fracture. Some of the complications causing poor function following Colles' fracture and methods of preventing or overcoming them will be discussed.

POST-TRAUMATIC FIBROSIS

Probably the most frequent cause of disability is the fibrosis produced in the soft tissues following prolonged swelling. Nearly all fractures are accompanied by hematoma formation or extravasation of blood as a result of

the trauma causing the injury. In addition, further swelling may be produced by the formation of traumatic edema fluid, either immediately after the injury or from mechanical causes interfering with the return circulation. Both hemorrhage and traumatic edema fluid are removed from the tissue spaces by the same processes, namely, absorption or organization. Absorption must take place within the first 7 to 10 days after the fracture, since organization proceeds at a rapid rate and is often well developed by the end of the second week. If organization occurs, fibrous bands are formed that may produce adhesions and interfere with the circulatory and lymphatic return flow. If formed near the joints, they limit movement and cause painful motion. In other areas, they cause the thick, brawny induration and shiny skin that is characteristic of these cases. The process of organization is concomitant with, and analogous to, the process of organization between bone ends that results in the formation of fibrous callus. In some instances, it may even eventuate in the deposition of calcium within the soft tissues; this is called myositis ossificans. I have never seen this near the wrist.

Since this process is simultaneous with bone healing, it is important that treatment for soft tissue damage be carried on while the bone is healing. Measures to assist the removal of edema fluid should be started as soon as the fracture is reduced. The best method of combating persistent swelling is motion of the muscles. Thus, there are two apparently antagonistic objectives to be attained at the same time; the fracture line must be continuously immobile to promote healing of the bone, while the muscles must be kept moving to assist the removal of edema and promote the function of the soft tissues. Both these objectives can be accomplished if a well-fitted but nonpadded plaster splint or cast is applied after adequate reduction and then trimmed for function. This means that the cast must be cut back to the flexion crease in the palm and behind the knuckle joints on the dorsum of the hand. In addition, the thumb must be trimmed so that opposition as well as flexion and extension are possible, since opposition is the most important movement of the thumb. The cast must be trimmed at the elbow, so that it will not interfere with flexion and extension, and if pronation and supination are desired, it must be trimmed considerably below the elbow. If this is done, even though the wrist may be in considerable flexion to maintain reduction, a great deal of function is possible throughout the healing period. The activity of normal function during the healing period is the best method of decreasing swelling in the normal physiological manner. Persistent efforts should be made to convince the patient that the injured hand may be used for normal daily functions, such as eating, dressing, combing hair, shaving, writing, opening and closing doors, and even for work,

if it does not involve heavy lifting or the immersion of the cast in water. Special instruction should be given that all three joints of each finger should be moved, the thumb should touch the little finger, and pronation and supination should be carried out with the elbow at right angles to prevent substitution of shoulder rotation for forearm rotation. The use of a sling should be discouraged, since activity is more feasible if the hand is available for constant use. If active motion is not effective, two other methods are available. The first is elevation. Usually, elevation has to be carried out with the patient in the recumbent position, with the extremity suspended from an overhead sling, since the ordinary sling, as worn in the erect position, does not reduce swelling, because it does not create a down grade all the way to the heart. However, exercise can be done at the same time. If neither of these methods is successful, heat and massage may be used to assist circulation and reduce swelling. A bivalved cast, half of which can be removed at a time to enable treatment during the acute stage, is usually worn. Great care must be taken with this method if the fragments are not to be displaced. Pain should never be produced during the acute stage of fracture. This method is more useful after the bone has healed, when there is no danger of displacing fragments; however, the likelihood of satisfactory results is greatly decreased if effective treatment is delayed until the bone has healed.

The shoulder is often involved in Colles' fracture. This is probably not due so much to direct trauma caused by falling on the shoulder or trauma produced by the force exerted through the arm to the shoulder as it is due to immobilization. The common practice of carrying the arm in a sling promotes such disability. In most cases, shoulder disability can be prevented by putting the hand behind the head and behind the back, daily. Putting the hand behind the head causes abduction and external rotation; putting the hand behind the back requires extension, adduction, and internal rotation. With these two exercises, all the more difficult movements are carried out. Occasionally, heat, massage, and exercise are necessary, particularly if activity has been limited during the early stages.

It is unfortunate that so many surgeons associate the term "physical therapy" with machine therapy. It is well known that physical therapy implies exercise, yet, in THE JOURNAL, the following statement was made by Cassebaum in an otherwise excellent report of a study of results in Colles' fracture: "When the splints were removed, active motion and exercises of the wrist were begun. These have a twofold purpose, namely, to increase motion and to redevelop the forearm muscles. Physical therapy was not used unless it was requested, and then its relative inferiority to active exercise was impressed on the patient. It was used for the occasional demoralized person who needed the feeling that something was being done for him and that others were interested. Through its more frequent contact with the patient was maintained. The daily application of moist heat proved helpful, and patients reported increased ranges of motion during this treatment."¹

If we were to adhere to a definition of "physical therapy" as meaning treatment by physical means, including rest and manipulation as well as exercise, the entire care of the fracture, including the reduction and application of the cast, consists of physical therapy.

We have so far been discussing prevention of post-traumatic fibrosis; however, many patients are seen by the physiatrist in the late stages, when this fibrosis is well established. In these cases, the use of heat, preferably whirlpool baths, followed by massage to reduce swelling, relieve pains, and stretch fibrous tissue, and then followed by exercise, using resistance exercises whenever possible, greatly expedites the return of function. Forcible manipulation, with or without anesthesia, is contraindicated as it increases the trauma and swelling and, therefore, defeats its own objective. Occupational therapy provides excellent forms of exercise that can be adapted to increase the range of finger and wrist motion and increase strength and skill; in addition it may hold the interest of the patient, so that he will work at it for longer periods and more effectively than at other forms of exercise.

Sudeck's acute post-traumatic bone atrophy occasionally follows Colles' fracture. I have seen one patient whom this occurred on two occasions, five years after following fracture of first one wrist and then the other. This condition is thought to be a reflex sympathetic dystrophy initiated by injury; it results in rapid bone atrophy. Roentgenograms show a spotty decalcification that may be severe enough to simulate tuberculosis. It is always accompanied by swelling and pain, even in the early stages. If activity is carried out from the beginning, this complication is extremely rare. The early performance of sympathetic block has been advised for these cases; however, I have usually not seen the patient early, and sympathetic block has been ineffective. The most effective treatment is activity, which is valuable in any manner that is feasible for the patient. Heat is contraindicated because it promotes bone atrophy. Electrical stimulation to produce muscle action may be of value in those cases in which the patient will not move the arm. This condition has a slow course, and the patient needs much encouragement during the recovery phase. As is common with other types of reflex sympathetic dystrophy, it occurs oftener in patients who are emotionally unstable, and this adds to the difficulties in their management. Occupational therapy is of great value, because it keeps the patient working longer a time than is usually possible with conventional exercises.

Post-traumatic arthritis not infrequently accompanies Colles' fracture. Mechanical changes may occur in the joint surfaces, but it is not known whether the arthritis is a result of the fracture. The immobilization that accompanies the fracture is a factor in promoting the change. It usually occurs in thin, bony, elderly patients and particularly in those patients who will not exercise or work if painful motions are necessary. After several months, roentgenograms show changes in the joint, consisting of cartilage loss and bone decalcification. The principles of treatment discussed under post-traumatic fibrosis are applicable here. It is usually difficult to tell when post-traumatic fibrosis ends and post-traumatic arthritis begins, for they may both be manifestations of the same process. In the thin, elderly patient, such as

1. Cassebaum, W. H.: Colles' Fracture, J. A. M. A. 143:963 (July 15) 1950.

plications should be anticipated and explicit instructions from the time of reduction should be given, along with frequent checking to see that the instructions are followed. Rare complications include rupture of the extensor pollicis longus tendon or other tendons, stenosing tendovaginitis, and involvements of the median or ulnar nerves causing paresthesias. Some of these require surgical repair.

SUMMARY

1. Some of the problems associated with the reduction and immobilization of Colles' fracture are discussed.
2. The principles of treatment of the following complications were explained: post-traumatic fibrosis, Sudeck's acute post-traumatic bone atrophy, post-traumatic arthritis, and tendon and nerve injuries.

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ELECTROLYTE SOLUTION APPROXIMATING PLASMA CONCENTRATIONS

WITH INCREASED POTASSIUM FOR ROUTINE FLUID AND ELECTROLYTE REPLACEMENT

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Recent studies have emphasized the desirability of maintaining normal levels of electrolytes and water in plasma and tissue cells. This is difficult to accomplish because the electrolyte composition of the primary replacement solutions generally available for parenteral therapy is significantly different from normal plasma. For example, 0.9% sodium chloride solution contains too much chloride but no bicarbonate and no potassium.

Attempts were made, therefore, to devise a water solution of plasma electrolytes to correct most anomalies. Animal experiments were conducted to obtain the first approximations, and then the proposed solution was subjected to clinical trial. The results to date have been sufficiently encouraging to warrant this report of our observations.

ANIMAL EXPERIMENTS

Hemorrhage was investigated first because of its ubiquity and importance in medicine and surgery and its reproducibility in dogs. Massive volumes of blood were removed from unanesthetized dogs and concurrently replaced with an electrolyte solution.¹ During and after the hemorrhage the hematocrit readings (red blood cell volume), plasma proteins, and electrolytes² of plasma and urine were determined at frequent intervals. The same procedure was repeated with the same dog one or more months later, with removal of blood and administration of electrolyte solution, but a solution with a different combination of electrolytes was utilized for replacement.

A typical series with one dog is summarized in Table 1. When the replacement solution contained sodium equal to chloride, as in 0.9% sodium chloride solution, infusions during massive hemorrhage lowered the Na:Cl ratio in the plasma. To maintain normal bicarbonate and chloride concentrations in the plasma during the massive hemorrhage, Na:Cl ratios in excess of 140:100 (1.4) were needed in the infusion solution.

In the urine the Na:Cl ratio declined to 1.0 or less when sodium chloride solution only was infused, but when the Na:Cl ratio in the infusion was 1.4 or greater, the Na:Cl ratio in the urine exceeded 1.0. The electrolyte balance data show that the retention of chloride exceeded the retention of sodium in all experiments with sodium

chloride solutions and emphasize the disadvantage of using chloride in replacement solutions in concentrations that are greater than the normal concentration of chloride in plasma.

Furthermore, after the massive removal of blood and its replacement with isotonic solutions of sodium salts only, the plasma potassium concentrations decreased markedly. Simultaneously, potassium equivalent to 10% to 20% of total body potassium was found in the large volumes of urine excreted. Thus in the experiments in Table 1 the total body potassium of the dog weighing 7 kg. is estimated to approximate 350 mEq., and urine potassium excretion after hemorrhage varied from 34 to 68 mEq. Graded additions of potassium to the sodium salt infusions showed that 10 mEq. per liter of solution approximated the minimum concentration that maintained plasma potassium at normal levels, although a negative balance of potassium still prevailed. In this connection it is noteworthy that decrease of plasma potassium was also observed in dogs dehydrated by loss of gastric juice and then rapidly rehydrated by infusions of sodium chloride only.³ A further observation in all experiments was that, although the total plasma protein was reduced to below 2 gm. per 100 cc. and infusions of sodium salts up to one-third of body weight were given, no detectable edema, peripheral or pulmonary, resulted.

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The balanced electrolyte solution was prepared by the Research Division of the Cutter Laboratories (Dr. Walter E. Ward, Medical Director) in accordance with our formula for experimental study and clinical trials.

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1. Fox, C. L., Jr., and Freeman, B. B.: Electrolyte, Nitrogen and Protein Changes That Follow Massive Removal of Red Cells and Plasma Protein, *Federation Proc.* 8: 49-50 (March) 1949.

2. Determinations of sodium and potassium in plasma, urine, and other biological samples were made with a stable internal standard flame photometer built in our laboratory. The construction, design and operation of this new instrument have recently been described in detail. (Fox, C. L., Jr.: Stable Internal Standard Flame Photometer for Potassium and Sodium Analyses, *Anal. Chem.* 23: 137 [Jan.] 1951). This instrument is obtainable from the Janke Aircraft Engine Test Equipment Company, Hackensack, N. J.

3. Van Slyke, K. K., and Evans, E. I.: Unpublished data cited by Van Slyke.²⁸

Since the toxicity of potassium is greatly enhanced in traumatic shock,⁴ additional experiments were performed to ascertain whether an isotonic solution of sodium salts with 5 mEq. of potassium per liter in excess of the normal plasma potassium level would prove harmful in potentially fatal shock with concomitant hyperpotassemia. Shock was produced by Rosenthal's technique of a two-hour application and release of tight tourniquets to both hind legs of mice. The classical signs of shock developed, including cyanosis, dyspnea, hypothermia, and hypotension, followed in 6 to 12 hours by a mortality of 98% to 100% in untreated animals.⁵ Treatment consisted of the administration in two divided doses of 150 cc. of solution per kilogram of body weight. The results are summarized in Table 2 and show that this isotonic

COMPOSITION OF BALANCED ELECTROLYTE SOLUTION

The composition of the balanced electrolyte solution as prepared for clinical studies is compared in Table 3 with normal human plasma⁷ and other commonly used intravenous replacement solutions (sixth-molar sodium lactate,⁸ Ringer's,⁹ lactated Ringer's,¹⁰ Darrow's,¹¹ and sodium chloride plus potassium chloride¹²). The sodium, calcium, magnesium, and chloride ions are present in their normal plasma concentrations.⁷

The remaining important anion, bicarbonate, is obtained chiefly from acetate which is very rapidly metabolized by the cells.¹³ Acetate in the solution is preferred over bicarbonate because it yields a neutral pH and is easily sterilized by boiling or autoclaving. Acetate is preferred over lactate because of its more rapid metabolic

TABLE 1.—Comparison of Effects of Various Replacement Solutions After Hemorrhage, Studied on Same Dog Over One Year

	Hema- to- crit Read- ing, %	Plasma					Urine				Infusion			
		Protein, Gm. %	mEq./Liter			HCO ₃ *	Vol., L.	Total mEq.			Vol., L.	Total mEq.		
			K	Na	Cl			K	Na	Cl		K	Na	Cl
First Experiment,† Wt. = 7.0 kg.														
Control 3/48	49	5.2		149	108	31		..	...	...		..	...	...
Post hemorrhage	13	1.4		150	135	5	0.86	17	125	136		..	...	...
15 hr. post hemorrhage.....	17	2.7		112	122	10	1.00	22	164	137		..	...	...
Totals/20 hr.	..	...		...	...	..	1.86	39	289	273	2.9	0	436	436
Net intake ‡	..	...		...	...	..		..	...	...	2.4	..	366	383
Balance	..	...		...	...	..	+ 0.54	- 39	+ 77	+ 110		..	...	...
Second Experiment,§ Wt. = 7.4 kg.														
Control, 5/48	43	5.8	4.76	149	113	26		..	...	...		..	...	...
Post hemorrhage	16	1.7	1.96	142	103	29	0.90	29	187	114		..	...	...
15 hr. post hemorrhage.....	15	3.1	3.64	139	120	9	0.91	39	95	37		..	...	...
Totals/20 hr.	..	...		...	...	..	1.81	68	282	151	2.55	0	382	216
Net intake	..	...		...	...	..		..	...	...	2.05	0	310	165
Balance	..	...		...	...	..	+ 0.24	- 63	+ 28	+ 14		..	...	...
Third Experiment, Wt. = 7.8 kg.														
Control 1/49	57	5.8	3.92	151	111	30		..	...	...		..	...	...
Post hemorrhage	19	1.4	3.50	135	108	17	0.31	13	54	34		..	...	...
15 hr. post hemorrhage.....	17	3.4	3.30	148	118	20	0.47	21	98	22		..	...	...
Totals/20 hr.	..	...		...	...	..	0.78	34	152	56	2.0	20	290	200
Net intake	..	...		...	...	..		..	...	...	1.5	19	220	150
Balance	..	...		...	...	..	+ 0.72	- 15	+ 68	+ 94		..	...	...

* Estimated by Na minus Cl plus 10 mEq., e. g., 149 minus 108 plus 10 equals 31.
† The solution infused was 0.9% NaCl, with 154 mEq. of Na and 154 mEq. of Cl per liter.
‡ Infusion minus intravascular fluid removed during exsanguination (red blood cells not included).
§ The composition of the solution was 150 mEq. of Na, 85 mEq. of Cl, and 65 mEq. of acetate per liter.
|| The composition of the solution was 140 mEq. of Na, 10 mEq. of K, 100 mEq. of Cl, and 50 mEq. of acetate.

solution with 10 mEq. per liter of potassium is not toxic. It should be noted that Rosenthal and Tabor⁶ demonstrated the toxicity of potassium in solutions devoid of sodium; furthermore, the toxicity of infused potassium is usually referred to in connection with a solution containing 30 mEq. per liter of excess potassium but hypotonic with respect to sodium (Na:K equals 3.5, Darrow's solution, Table 3).

conversion to bicarbonate in the body. Lactate ordinarily is used as the racemic mixture of d- and l- forms, and the relatively slow metabolism of the l- form¹⁴ may possibly account for the not inconsiderable loss in the urine.¹⁵ The small amount of citrate added to obtain some inhibition of clotting in the needle during slow infusions provides an additional source of base, so that bicarbonate in the form of precursors totaling 55 mEq. per liter is present in twice its normal plasma concentration.

Potassium is also present in twice its normal plasma concentration to expedite replenishment of intracellular losses. Consequently each liter of the solution provides an excess, above that needed to make up normal plasma extracellular fluid, of 5 mEq. of potassium and 28 mEq. of available fixed base, i. e., sodium, potassium, calcium or magnesium not present as chloride or other anion requiring removal via the kidneys. The fixed base is available to neutralize fixed acid radicals such as phosphoric

4. Rosenthal, S. M., and Tabor, H.: Electrolyte Changes and Chemotherapy in Experimental Burn and Traumatic Shock and Hemorrhage, Arch. Surg. 51: 244-252 (Nov.-Dec.) 1945.
5. Footnote 4. Rosenthal, S. M.: Experimental Chemotherapy of Burns and Shock: IV. Production of Traumatic Shock in Mice; V. Therapy with Mouse Serum and Sodium Salts, Pub. Health Rep. 58: 1429-1436 (Sept. 24) 1943.
6. Footnote 4. Tabor, H., and Rosenthal, S. M.: Experimental Chemotherapy of Burns and Shock: Electrolyte Changes in Tourniquet Shock, Pub. Health Rep. 60: 401-419 (April 13) 1945.
7. Gamble, J. L.: Chemical Anatomy, Physiology and Pathology of Extracellular Fluid: A Lecture Syllabus, ed. 5, Cambridge, Mass., Harvard University Press, 1947.

and sulfate. Because the tissue cells contain bicarbonate, correction of acidosis inside and outside the cells may be facilitated by supplying cells with a readily metabolized precursor of bicarbonate.

Calcium is included to aid in maintaining its normal plasma level, to counteract the inhibitory effect of potassium on the heart,⁹ and to avoid the complications provoked by administering potassium during hypocalcemia.¹⁶ It is also of value in avoiding hypocalcemic tetany per se, especially in patients with renal insufficiency, which is frequently associated with hypocalcemia and hypopotassemia.¹⁷

Magnesium is present to help maintain its normal plasma level and to prevent disturbances of neuromuscular function, especially tetany,¹⁸ to replenish cell losses, and to assist in the activation of important intracellular enzymes, which requires optimum concentrations of this ion.

Furthermore, potassium, calcium, and magnesium ions and sodium acetate have been observed to induce a

TABLE 2.—Treatment of Acute Tourniquet Shock* in Mice with Balanced Electrolyte Solution† Containing 10 mEq. per Liter of Potassium

	Controls	Treated
No. Mice.....	30	25
No. Died.....	29	1
Mortality, %.....	97	4

* Shock was produced by the two-hour application and release of bilateral tight tourniquets to the hind legs of mice as described by Rosenthal.⁵

† Treatment consisted of the intraperitoneal injection of 150 cc. per kilogram body weight of this solution; thus a 20 gm. mouse received 2 cc. one hour after removal of the tourniquets and 1 cc. four hours later. An additional group of 30 mice in shock received this electrolyte solution containing 5% of glucose. The presence of the glucose greatly retarded absorption of the fluid; only 6 of the mice survived and the peritoneal cavity of the dead mice contained a volume of fluid equal to that injected. The glucose electrolyte solution was then administered intravenously to a small group of mice in shock and all survived; successful intravenous treatment of mice in profound shock is technically difficult and was not further studied.

diuretic action¹⁹; their presence in the solution serves to enhance diuresis of excess water and to prevent lowering their plasma levels by dilution.

CLINICAL STUDIES

Because of its ionic similarity to plasma, balanced electrolyte solution in large infusions will expand the volume of plasma and extracellular fluid without distorting their ionic composition. The additional potassium and acetate are miscible with the vastly greater volume of intracellular fluid. Thus this solution differs markedly from 0.9% sodium chloride solution, Ringer's solution, or dextrose in water solutions, which of necessity exaggerate abnormalities in the composition of body fluids they are administered to replace.

The distortions caused by the 0.9% sodium chloride solution were demonstrated in patients who received 8,000 cc. of each solution postoperatively at eight day intervals. Comparisons of plasma concentrations show elevation of chloride and decrease in bicarbonate following infusion of 0.9% sodium chloride solution, but no significant changes following similar balanced electrolyte solution infusions. An example of such an experiment is shown in Table 4. Despite the similarity of potassium excretion after either infusion, balanced electrolyte solution, but not 0.9% sodium chloride solution, compensated for the potassium excreted.

Losses of intracellular potassium have been observed in numerous medical²⁰ and surgical disorders,²¹ and hypopotassemia has been described frequently.²² Inasmuch as major surgical procedures are followed by considerable excretion of potassium in the urine,²³ more complete replacement with balanced electrolyte solution was tried. A typical experience following a rather difficult subtotal gastrectomy is shown in Table 5. Although a negative potassium balance prevailed for the first few days postoperatively, hypopotassemia did not occur and a positive balance ensued. Experience with balanced electrolyte solution was obtained with a large group of surgical patients during a study of postoperative hypopotassemia and hyperpotassuria.^{21b} The effects of the administration of the solution on the renal excretion of water and electrolytes following gastrectomy and similar major surgical procedures are shown in Table 6, which summarizes the average daily values in 18 patients.

It is apparent that adequate volumes of urine and large amounts of sodium and chloride were excreted, even in the first few days following operation. It is noteworthy that in all instances the concentration of sodium exceeded that of chloride.

The initial hyperpotassuria is apparent, but in the later days the daily excretion of potassium fell to below normal, suggesting the beginning of retention and cellular replenishment. It is important to contrast the high urinary excretion of sodium and chloride in these patients following infusion of balanced electrolyte solution with the low concentrations—usually with sodium lower than chloride—following administration of various mixtures of 0.9% sodium chloride solution and dextrose and water.^{23b}

In the presence of impaired kidney function, solutions containing potassium should be used cautiously. The

8. Hartmann, A. F., and Senn, M. J. E.: Studies in Metabolism of Sodium *r*-Lactate: Response of Normal Human Subjects to Intravenous Injection of Sodium *r*-Lactate, *J. Clin. Invest.* **11**: 327-335 (March) 1932; Studies in Metabolism of Sodium *r*-Lactate: Response of Human Subjects with Acidosis to Intravenous Injection of Sodium *r*-Lactate, *ibid.* **11**: 337-344 (March) 1932; Studies in Metabolism of Sodium *r*-Lactate: Response of Human Subjects with Liver Damage, Disturbed Water and Mineral Balance, and Renal Insufficiency to Intravenous Injection of Sodium *r*-Lactate, *ibid.* **11**: 345-355 (March) 1932.

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comparative safety of balanced electrolyte solutions is attested by numerous clinical trials in patients with renal insufficiency, oliguria, and uremia. One example is given in Table 7. After intravenous administration of large volumes of the solution to an elderly patient in uremia with vomiting, abdominal distention, and diarrhea, oliguria was changed to polyuria, acidosis was corrected, the blood urea nitrogen level was brought down to normal, and hypopotassemia gradually was overcome. Furthermore, no signs of pulmonary congestion or edema occurred, despite the massive infusion of both sodium and fluid.

The over-all clinical trials to be reported in detail elsewhere can be briefly summarized. Over 700 liters of balanced electrolyte solution, often containing 5% of dextrose, have been administered intravenously to patients at Flower and Fifth Avenue Hospitals after gastrectomy, abdominal-perineal resections, and other major surgical procedures. In the limited experience to date, the use of 3,000 cc. daily of this new solution seemed to prevent postoperative potassium deficiency as judged by plasma analyses and clinical observation, even though considerable potassuria occurred during the first postoperative days.^{21b} Plasma concentrations of sodium,

Potassium acetate is preferable to potassium chloride for intracellular replacement, since the problem of the disposal of the unwanted chloride ion is avoided.²³

The urinary outputs (Table 6) have been unusually high despite the poor condition of many patients and the extensive surgical procedures performed. Postoperative salt and water retention did not occur. Edema, peripheral or pulmonary, has not been noted. After infusion of 3,000 cc. of balanced electrolyte solution preoperatively and postoperatively, significant chloride retention was not observed postoperatively; some patients retained less salt after operation than before. In contrast, Ariel²⁸ using infusions of 0.9% sodium chloride solution in this way found greater salt retention postoperatively.

In pediatric patients with acute diarrheal disease, diabetic or renal acidosis, or dehydration associated with acute infections, the use of 50 to 150 cc. per kilogram of body weight restored normal hydration, avoided hypopotassemia, and yielded normal plasma electrolyte values. Tetany and alkalosis did not occur. In extremely severe acidosis, sufficient evidence is not yet available to indicate whether sixth-molar sodium lactate can be dispensed with and sole reliance placed on balanced elec-

TABLE 3.—Comparison of New Solution with Plasma and Other Replacement Solutions

	Plasma †	Balanced Electrolyte Solution	All Concentrations in mEq./L.			U.S.P.* Lactated Ringer's Solution ¹⁰	Darrow's Solution ¹¹	NaCl Plus KCl ¹²
			0.9% NaCl	M/6 Sodium Lactate Solution ⁹	U.S.P.* Ringer's Solution ⁹			
Na +	140	140	154	167	147	130	122	110
Cl -	103	103	154	0	155.5	109	104	110
HCO ₃ -	27	55 †	0	167 ‡	0	28 †	53 †	0
K +	5	10	0	0	4	4	35	30
Ca ++	5	5	0	0	4.5	3	0	0
Mg ++	3	3	0	0	0	0	0	0

* U.S.P. formulas in general use are slightly different than the concentrations in footnotes 9 and 10.
† Obtained by metabolism of acetate 17 and citrate 8.
‡ Obtained by metabolism of racemic lactate.

bicarbonate, and chloride were also adjusted and maintained close to normal.

Since it is not to be expected that this solution will provide sufficient potassium for the correction of pre-existing massive deficiencies, higher concentrations can be obtained readily by addition of concentrated potassium acetate²⁴ to the solution. For example, in Table 7 the patient on several occasions required 25 to 100 mEq. of additional potassium acetate per day in the infusions.

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22. Footnote 12. Danowski.^{20b}

23. (a) Wilkinson, Billing, Nagy, and Stewart.^{21a} (b) Elman, R.; Lemmer, R. A.; Weichselbaum, T. E.; Owen, J. G., and Yore, R. W.: Minimum Postoperative Maintenance Requirements for Parenteral Water, Sodium, Potassium, Chloride and Glucose, *Ann. Surg.* **130**: 703-722 (Oct.) 1949.

24. Sterile 10 cc. ampules containing 5 mEq. per cubic centimeter of potassium acetate were supplied by the Cutter Laboratories; addition of 5 cc. to 1 liter of balanced electrolyte solution raises the concentration of potassium to 35 mEq. per liter.

trolyte solution to restore plasma bicarbonate and pH to normal.²⁷

TABLE 4.—Comparison of Effects of Massive Infusions* of 0.9 Per Cent Sodium Chloride and Balanced Electrolyte Solution on Plasma and Urine Electrolytes

Time, Hr.	Plasma Concentrations, mEq./L.								Hemato- crit, %		
	Na		Cl		HCO ₃		K				
	NaCl	BES†	NaCl	BES	NaCl	BES	NaCl	BES	NaCl	BES	
0	0	140	146	104	105	22	15	4.8	4.0	50	49
4	4	137	148	115	112	19	23	4.0	4.0	41	47
7 §	11	150	154	120	108	13	22	4.5	4.3	42	40
24	22	150	150	106	108	20	20	4.0	4.0	49	50
Urine Concentrations											
12	12	156	176	175	118	..	..	19	18	..	..

* Both infusions were 8,000 cc. and were given intravenously at the rate of 1,000 cc. per hour to a patient weighing 73 kg.
† NaCl = 0.9% sodium chloride solution, administered Oct. 2.
‡ BES = balanced electrolyte solution, administered Sept. 23.
§ Convulsive movements and facial edema observed.

Urologic patients frequently present reduced plasma sodium, together with acidosis, hypopotassemia, and varying degrees of renal insufficiency resulting from several types of urinary tract obstruction and disease. Clinical results such as those shown in Table 7 have been obtained. Although most of the patients were over 65 years of age, pulmonary edema did not occur.

In a series of patients undergoing multiple orthopedic surgical procedures, 2 to 4 liters have been used for one or more days preoperatively and postoperatively. Normal fluid and electrolyte balances were obtained with minimal laboratory control. It may be noteworthy that the patients who received supplementary oral fluids excreted urine with much lower concentrations of electrolytes than the surgical patients represented in Table 6.

In all, approximately 100 patients have each received 3 to 25 liters of this solution. No signs of potassium toxicity, tetany, or metabolic alkalosis have been observed. Elevated plasma carbon dioxide values have been obtained occasionally, the maximum value being shown in Table 7. In this connection it is of interest that the potential bicarbonate concentration of this solution is similar to that recommended by Darrow²² (Table 3).

COMMENT

Van Slyke²⁸ has referred to 0.9% sodium chloride solution as "unphysiological saline," since it contains 50% more chloride than the plasma. Infusions of saline solution distort the composition of body fluids to some degree and provide no available fixed base until renal activity removes the chloride as ammonium or potassium

to 102 mEq. per liter) may account in part for the low plasma sodium values discernible in their patients.^{30a} Additional clues are Wilde's²⁹ experiments indicating a shift of chloride into muscles deficient in potassium and the finding of excess chloride in potassium-depleted muscles obtained at autopsy from children with the nephrotic syndrome.³²

Inclusion of calcium, magnesium, and potassium in the solution sustains the plasma levels of these ions and takes advantage of their diuretic action. The copious urinary outputs observed may represent the renal response to one or more of these ions or to the expansion of plasma and extracellular volume without ionic distortion. The enhancement of renal tubular transport by acetate³³ may also be a factor. Detailed studies of these effects are needed. The role in renal function of excess bicarbonate and of the other factors mentioned in designing balanced electrolyte solution has been reviewed by Pitts³⁴ and Wolf³⁵ and applied clinically by Fox and McCune (Table 7).

In some of our hemorrhage experiments¹ and in at least one published study of diabetic acidosis,³⁶ the urine data suggested that, after administration of 0.9% sodium chloride solution, subsequent potassuria might represent

TABLE 5.—Example of Postoperative Therapy with Balanced Electrolyte Solution After Subtotal Gastrectomy in Patient Aged Fifty-Five

Postoperative Day	Therapy, L.	Plasma K (mEq./L.)	Volume, L.	Creatinine, Gm.	Daily Urine Output				
					Total mEq.			N, Gm.	K/N
					Na	Cl	K		
Preoperative.....		5.04		...	...	...	...		...
1 & 2 (48 hr.).....	Blood, 1			...	...	...	...		...
	D/H ₂ O, 1		1.93	4.3	814	180	171	27.3	6.2 †
	BES,* 4			...	...	...	...		...
3.....	BES,* 3	4.3	1.25	2.3	325	190	80	12.9	6.1
4.....	BES,* 2		1.03	1.9	202	151	45	13.6	8.3
5.....	Oral milk, etc.	4.0	1.55	2.0	301	244	32	10.3	1.9
6.....	Oral milk, etc.		0.7	1.7	81	53	20	12.2	1.6
7.....	Oral milk, etc.		0.9	2.0	100	83	23	15.6	1.8
8.....	Oral milk, etc.	5.12	1.0	1.8	132	121	35	15.3	2.3

* The balanced electrolyte solution (BES) used contained 5% dextrose.
† The K/N ratio in the first 18 hours postoperatively has usually exceeded 10, indicating a disproportionately greater loss of K.

chloride¹² (unless the chloride ion enters cells²⁹). For these reasons the use of 0.9% sodium chloride solution may well be responsible for some of the difficulties and

an attempt by the body to excrete the excess of infused chloride without sodium; frequently the urine chloride equaled the sum of sodium plus potassium excreted. Likewise, when sodium chloride solutions are supplemented with potassium chloride,¹² a similar trend to excessive potassium excretion is discernible. The poten-

TABLE 6.—Composition of the Urine* Following Postoperative Administration of Balanced Electrolyte Solution

	Day of Operation†	Postoperative Days‡				
		1	2	3	4	5
Urine vol., cc.....	1,060	1,500	1,510	1,500	1,470	1,320
Sodium, mEq.	183	237	212	202	228	270
Chloride, mEq.	160	190	182	177	166	215
Potassium, mEq.	88	75	48	33	25	23

* Values are averages of total milliequivalents per day voided by 13 patients who received 2,000 to 3,000 cc. daily of balanced electrolyte solution after gastrectomy, abdominal-perineal resection, or other major operations. Data of eight different cases have been published.^{21b}
† The interval from the end of operation to the next morning ranged from 10 to 20 hours.
‡ These are 24-hour collections.

translocations in postoperative fluid therapy described by Collier, Moyer,³⁰ and others.³¹ A further clue is their preference for a 0.5 to 0.6% solution of sodium chloride, which provides chloride ion in normal plasma or extracellular fluid concentrations. The fact that such solutions are markedly hypotonic with respect to sodium (Na=85

25. Recent studies (Gamble, J. L., and others: Effects of Large Loads of Electrolytes, *Pediatrics* 7: 305 [March] 1951) "suggest that KCl is not a suitable salt to use for replacement of loss of intracellular fluid incurred by dehydrating processes."
26. Ariel, I. M., and Kremen, A. J.: Compartmental Distribution of Sodium Chloride in Surgical Patients Pre- and Postoperatively, *Ann. Surg.* 132: 1009-1026 (Dec.) 1950.
27. Hartmann, A. F.: Treatment of Severe Diabetic Acidosis: Comparison of Methods, with Particular Reference to Use of Racemic Sodium Lactate, *Arch. Int. Med.* 56: 413-434 (Sept.) 1935.
28. Van Slyke, D. D.: Effects of Shock on Kidney, *Ann. Int. Med.* 28: 701-722 (April) 1948.
29. Wilde, W. S.: Chloride Equilibrium in Muscle, *Am. J. Physiol.* 143: 666-676 (May) 1945.
30. (a) Collier, F. A.; Campbell, K. N.; Vaughan, H. H.; Iob, L. V., and Moyer, Carl A.: Postoperative Salt Intolerance, *Ann. Surg.* 119: 533-542 (April) 1944. (b) Collier, F. A.; Vaughan, H. H.; Kalder, N. B., and Moyer, C. A.: Translocation of Fluid Produced by Intravenous Administration of Isotonic Salt Solutions in Man Postoperatively, *ibid.* 122: 663-677 (Oct.) 1945.
31. Johnson, H. T.; Conn, J. W.; Iob, L. V., and Collier, F. A.: Postoperative Salt Retention and Its Relation to Increased Adrenal Cortical Function, *Ann. Surg.* 132: 374-385 (Sept.) 1950.

tial usefulness of balanced electrolyte solution in the treatment of diabetic acidosis can be indicated by reviewing Holler's case report of potassium deficiency with paralysis.^{30a} Had this patient received infusions of balanced electrolyte solution equal to the large amounts of sodium chloride and sodium lactate solutions administered, the potassium intake would automatically have approximated that ultimately given to overcome the symptoms of potassium deficiency which followed the initial infusions of sodium salts only.

To replace the losses that occur in diarrheal disease, Darrow introduced the use of larger amounts of potassium in replacement solutions.³⁷ Subsequent studies emphasized that the recommended solution, containing 35 mEq. per liter of potassium, imposed the hazard of potassium toxicity,³⁸ and Darrow has advocated that

semia resulting from dilution of extracellular fluid with saline, lactate, or other non-potassium-containing solutions. Some of the difficulties of regulating potassium therapy by the electrocardiogram have been described.⁴⁰ Extensive laboratory and clinical studies have shown that, in numerous fluid and electrolyte problems in medicine and surgery, replacement of extracellular fluid with its quota of available free base is of primary importance.⁴¹ To approximate extracellular fluid, a mixture of two-thirds 0.9% sodium chloride solution and one-third sixth-molar sodium lactate solution was advised in the treatment of severe burns after the initial sodium loss and acidosis had been corrected with sixth-molar sodium lactate.⁴² This mixture was subsequently recommended for use either by mouth or parenterally in the treatment of burn shock by the Subcommittee on Shock of the Na-

TABLE 7.—Prolonged Use of Balanced Electrolyte Solution and Supplementary Potassium Acetate in Elderly Uremic Patient with Prolonged Vomiting and Diarrhea

Date	Blood		Plasma					Urine Output *			Intravenous Intake †			
	Urea N, Mg./100 Ce.	Hemato- crit, %	Protein, Gm./100 Ce.	mEq./L.				Vol., Ce.	Total mEq.		Vol., Ce.	Total mEq.		
				Na	Cl	CO ₂	K		Na	K		Na	Cl	K
11/18	83	47	8.5	150	100	19	3.65	500	5	..	2,200	0	0	0
11/20 †	137	50	8.0	136	90	22	4.7	700	11	56	3,000	73	73	0
..	..	60	..	125	89	22	3.5	500	..	..		0	0	0
Therapy with BES Begun														
11/21	..	..	..	..	..	..		4,900	55	120	3,100	420	315	30
11/22	..	..	..	..	..	..	3.0		..	..	2,000	280	210	20
11/23	..	..	..	..	..	..			..	..	3,000	420	315	30
11/24	81	..	..	160	..	..	3.2	1,000	0	37	3,700	280	210	48
11/25	74	41	7.0	162	101	37		1,000	44	72	2,900	140	105	68
11/26	46	..	..	..	105	36		1,270	72	83	3,500	140	105	40
11/27	..	..	..	155	..	..	2.75	1,050	83	38	2,700	210	158	95
11/28	..	..	..	151	..	..	2.95	1,300	135	34	3,000	280	210	45
11/29	..	..	..	151	..	..	2.95		..	..	2,500	280	210	20
11/30	..	..	..	150	..	..	2.85		..	..	2,400	140	105	35
12/1	13	37	6.0	146	109	24	3.05	1,100	104	33	1,650	140	105	35
12/2	..	..	..	137	..	..			..	..	3,100	420	315	30
12/3	..	..	..	..	..	..			..	..	3,500	140	105	35
12/4	26	..	..	110	..	..	3.1		..	..	4,000	420	315	70
12/5	..	..	..	117	..	..	3.1		..	..	4,000	420	315	80
12/6	..	..	..	..	..	..		1,280	170	22	3,000	280	210	70
12/7	..	..	..	..	..	..			..	..		...	...	..
12/8	13	..	..	139	101	23			..	..		...	...	..

* Output data do not include large losses of 100 to 5,000 cc. via nasogastric and Miller-Abbott tubes for many days. Note the adequate urine output and constantly decreasing blood urea nitrogen level achieved with rising plasma levels of sodium and bicarbonate (Fox, C. L., Jr., and McCune, D. J.: Electrolyte Changes in Nephrosis: Occurrence of Diuresis Following Administration of Sodium and Potassium Salts, *Am. J. M. Sc.* 216:1-10 [July] 1918).

† Some dextrose and water was given at times, hence fluid intakes are greater than corresponding electrolyte intakes.

‡ First line, a.m.; second line, p.m.

most of the required potassium be replaced by oral therapy after the acute episode.³⁹ This hazard is avoided with balanced electrolyte solution which permits early administration of potassium and prevents hypopotas-

sia resulting from dilution of extracellular fluid with saline, lactate, or other non-potassium-containing solutions. Some of the difficulties of regulating potassium therapy by the electrocardiogram have been described.⁴⁰ Extensive laboratory and clinical studies have shown that, in numerous fluid and electrolyte problems in medicine and surgery, replacement of extracellular fluid with its quota of available free base is of primary importance.⁴¹ To approximate extracellular fluid, a mixture of two-thirds 0.9% sodium chloride solution and one-third sixth-molar sodium lactate solution was advised in the treatment of severe burns after the initial sodium loss and acidosis had been corrected with sixth-molar sodium lactate.⁴² This mixture was subsequently recommended for use either by mouth or parenterally in the treatment of burn shock by the Subcommittee on Shock of the Na-

Solutions similar to balanced electrolyte solution were proposed many years ago by Ringer⁹ and Hartmann,¹⁰ but they have not been used as extensively as isotonic sodium chloride solution. Obviously 0.9% sodium chloride solution is the simplest solution to prepare, and some surgeons have found it efficacious.⁴⁵ There is now much evidence that it is not the best solution for replacement or supportive therapy. Its lack of both potassium and available base seems to be a serious deficiency, especially when large volumes of solution are required. Further-

32. Fox, C. L., Jr., and Slobody, L. B.: Tissue Changes in Nephrotic Syndrome: Demonstration of Potassium Depletion, *Pediatrics* 7:186-192 (Feb.) 1951.

33. Mudge, G. H., and Taggart, J. V.: Effect of Acetate on Renal Excretion of p-Aminohippurate in Dog, *Am. J. Physiol.* 161:191-197 (April) 1950.

34. Pitts, R. F.: Acid-Base Regulation by Kidneys, *Am. J. Med.* 9:356-372 (Sept.) 1950.

35. Wolf, A. V.: The Urinary Function of the Kidney, New York, Grune & Stratton, 1950.

36. Danowski, T. S.; Peters, J. H.; Rathbun, J. C.; Quashnock, J. M., and Greenman, L.: Studies in Diabetic Acidosis and Coma, with Particular Emphasis on Retention of Administered Potassium, *J. Clin. Invest.* 28:1-9 (Jan.) 1949.

37. Darrow, D. C.: Retention of Electrolytes During Recovery from Severe Dehydration Due to Diarrhea, *J. Pediat.* 28:515-540 (May) 1946.

38. Govan, C. D., Jr., and Weiseth, W. M.: Potassium Intoxication: Report of Infant Surviving Serum Potassium Level of 12.27 Millimoles per Liter, *J. Pediat.* 28:550-553 (May) 1946.

39. Darrow, D. C.: Disturbances in Electrolyte Metabolism in Man and Their Management, *Bull. New York Acad. Med.* 24:147-165 (March) 1948.

more, the absence of both calcium and magnesium is not desirable.

Further study is necessary, but examination of Table 3 suggests the logic of using a solution patterned after plasma; our present experience indicates the additional usefulness of supplementary available fixed base and potassium.

At a time when blood substitutes are in short supply, it would seem advisable to study carefully a solution that simulates plasma and extracellular fluid much more closely than 0.9% sodium chloride solution or dextrose in water.

SUMMARY AND CONCLUSIONS

A physiological electrolyte replacement solution which contains sodium, calcium, magnesium, and chloride ions in the normal plasma concentrations is described. Its potassium concentration of 10 mEq. per liter is twice the normal plasma value; likewise, bicarbonate is provided in twice its plasma concentration in the form of rapidly metabolizable precursors, acetate and citrate. The rationale for the use of this solution with available free base and potassium is presented.

In managing the electrolyte and fluid therapy of surgical, pediatric, orthopedic, and urologic patients who lose intracellular potassium after extensive operative procedures or disease, substitution of this solution for 0.9% sodium chloride solution or other solutions has restored acid-base balance and prevented the occurrence of hypokalemia. The physiological ratio of sodium to chloride and the available free base in this new solu-

tion prevent chloride and fluid dislocations, thus avoiding postoperative oliguria and sodium chloride retention.

Experimental and clinical data indicate that this single physiological solution prevents postoperative hypokalemia without danger of toxicity, corrects moderate acidosis without inducing alkalosis, replaces the electrolytes in extracellular fluid, and induces copious secretion of urine and salt.

The solution is readily available for trials by others, who may thereby discover improvements (e. g., that the potassium concentration can be raised without incurring toxicity) and perhaps confirm our impression that elimination of 0.9% sodium chloride solution and other "unphysiological" solutions now in general use will greatly simplify and improve fluid and electrolyte therapy and thereby prevent the development of electrolyte abnormalities, iatrogenic or otherwise.

Fifth Ave. at 105th St. (Dr. Fox).

40. Currens, J. H., and Crawford, J. D.: Electrocardiogram and Disturbance of Potassium Metabolism, *New England J. Med.* **243**: 843-850 (Nov. 30) 1950.

41. Darrow, D. C., and Pratt, E. L.: Fluid Therapy: Relation to Tissue Composition and Expenditure of Water and Electrolyte, *J. A. M. A.* **143**: 365-373 (May 27); 432-439 (June 3) 1950.

42. Fox, C. L., Jr.: Oral Sodium Lactate in Treatment of Burn Shock, *J. A. M. A.* **124**: 207-212 (Jan. 22) 1944.

43. Harkins, H. N.; Cope, O.; Evans, E. I.; Phillips, R. A., and Richards, D. W.: Fluid and Nutritional Therapy of Burns, *J. A. M. A.* **128**: 475-479 (June 16) 1945.

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PSYCHOLOGICAL PROBLEMS OF ADJUSTMENT TO CANCER OF THE BREAST

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This paper is the result of a joint investigation by a group of psychoanalysts and surgeons, headed by Dr. Catherine Bacon of the Chicago Institute for Psychoanalysis and Dr. Max Cutler of the Chicago Tumor Institute. Our problem was an exploratory study of the possible psychosomatic aspects of cancer of the breast. The results of this research will be published in a subsequent joint communication. One of us (R. R.) was particularly impressed by the surgeon's interest in the problem of how, why, when, and what to tell the patient with breast carcinoma. The problem was sharply focused during observation of the emotional reactions of 50 women operated on by one of us (M. C.) to the handling by their referring or staff physicians. Our paper is an outgrowth of this analyst's observations and incorporates within it the surgeon's practical experience in the correct, intuitive emotional management of his many cancer patients in the past.

In the development of almost every field of science a periodic point is reached at which that particular group is not currently integrating or utilizing its total research advancements or parallel ones in auxiliary fields. The

time lag is costly to both physician and patient. This inertia is due to the slow recognition, absorption, and integration of advances from widely scattered sources of research. It is also augmented within the medical profession by the isolation of specialist groups from one another. This contributes to a focal, rather than a total, view of an existing problem. Thus, two detached bodies—surgeons and psychoanalysts—can work within the same hospital, but because of the narrowness of their specialties fail to interchange valuable pieces of new or even old knowledge. We feel that such a state of inertia exists in the psychological handling of women with breast cancer and that here is a situation with potentially, severe emotional trauma that is being sadly mismanaged and misunderstood by a good percentage of the medical profession.

It is our purpose to correlate the status of current surgical treatment of cancer of the breast with applicable psychoanalytic knowledge of behavior. This approach is directed toward a logical viewing of our patient as a total personality invaded by a malignant disease process. We are concerned with the psychological meaning of the

breast and an understanding of the range of emotional shock associated with breast destruction. Our interest is also centered in the surgeon's significant role in his patient's life and in the emotional impact of the cancer upon the surgeon. We hope to gain some appreciation of the psychological interaction between patient and surgeon, and as an outgrowth of this to propose a general method for the emotional management of women with breast cancers.

The problems are best approached through a basic exploration of the dual psychological conflict confronting a woman with breast cancer: (1) adjustment to breast mutilation, and (2) adjustment to invasion by a potentially deadly disease.

ADJUSTMENT TO BREAST MUTILATION

Postmastectomy depression was noted as a frequent reaction in the group we studied. This is a more or less common sequel to mastectomy and is marked by anxiety, insomnia, depressive attitudes, occasional ideas of suicide, and feelings of shame and worthlessness. The depression is characterized by its emotional similarity to mourning. One can say that these women mourn the loss of their breast. They are concerned with what their husbands, or men in general, will think of them in their new mutilated state. Feminine pride has been severely damaged. They are faced with the problem of changing the mind's picture of their body image to one with a unilateral breast, or perhaps none at all.

We can better understand something of the background of this depressive reaction if we consider the emotional meaning of the breast within a woman's total personality. Breasts are among her most prized physical possessions. They have two major psychological meanings. First of all, in our culture, breasts have a particular sexual significance. They are glamorized in magazines, street car ads, and the movies. Women and men have been made more and more breast conscious. In fact, when we examine the situation critically we see that the breasts are the only positive evidence of femaleness. The reproductive organs are internal, and the pubic area is smooth and concealed. Remove a woman's breasts and she has lost her badge of femininity. Psychologically it has the same qualitative meaning as loss of the penis in man. This is often demonstrated in dreams and neurotic symptomatology wherein both men and women tend to equate the penis with the breast.

The other major meaning of the breast lies in its function as a milk-bearing organ. It is equated with something that is uniquely female—the role of a mother. In our culture this has become superficially less important, since fewer mothers pride themselves on their ability to breast feed. This is, however, emotionally misleading, since there remains an unshakable and universally unconscious symbolic connection between the breast and motherhood. The breast, therefore, is the emotional symbol of the woman's pride in her sexuality and in her motherliness. To threaten the breast is to shake the very core of her feminine orientation.

The surgeon has to be acutely aware of these dual meanings of the breast. He must understand that the primary emotional reaction connected with disease of the

breast usually is not a fear of cancer or death, but is rather the shocking feeling that the basic feminine role is in danger. This frequently results in "ostrich-like" behavior, through which the woman postpones going to her doctor about the discovered lump. The original emotional trauma, then, most often occurs on the level of the woman's realization that her femininity is endangered. It is, of course, immediately mixed with the concept of cancer and its potential threat to life, but this does not emerge as the central problem of adjustment until later, after she has become accustomed to the inevitability of mutilation and managed to attain some sort of psychological adjustment to her new physical self. Her first problem is that of protecting her breast; only later does she begin protecting her life. It is obvious that the surgeon cannot wait for this transition to occur, but must bear in mind that the emotional focus is different in the preoperative and postoperative periods than in the latter convalescent and radiation-therapy phases, when the threat to life becomes the struggle.

Is there any way in which he can gauge the intensity of this initial reaction? We believe that there is.

PSYCHOLOGICAL MANAGEMENT

Women exhibit wide variations in conscious attitudes to their breasts, ranging from extreme pride through indifference to excessive shame. These emotional reactions are partially conditioned by the actual physical appearance of the breasts, whether they are well-shaped or unsightly, but primarily they stem from deep psychological attitudes of acceptance or denial of the fundamental feminine role, i. e., sex and motherhood.

The mature woman accepts her breasts, good or bad, with a proportionate amount of pride and utilizes them to their best cosmetic and sexual advantage. She does not feel attitudes of indifference or shame. Later in life—after successful marriage, motherhood, and the climacteric—her breasts have less dynamic significance. She then has other evidence of her prowess, i. e., a husband and children, and is more ready to accept a future in which little emphasis is placed on the sexual and maternal role of her breasts. We can say that they have served their purpose and she is now ready to accept their retirement. Her feelings over loss of a breast at this later age are as proportionately different as the degree of mourning one would expect over the death of a husband in his prime or after his late retirement from an active, full, and accomplished life.

The climacteric period is a time when old problems over femininity may once more emerge. She also is normally confronted with the problem of adjusting to cessation of fertility. Some women feel that the menopause will rob them of their sexual allure. Loss of the breast, therefore, in this phase of life increases the problem of adjustment. Again the difficulty is less in women with a history of successful feminine functioning as previously outlined.

We deduce from this that in the emotionally mature woman the greatest trauma from cancer and breast amputation occurs during the preclimacteric and climacteric periods, when it threatens the fulfillment of her optimal feminine functioning. The trauma tends to be greater in

direct proportion to her comparative youth and to the degree of feminine achievement that she feels she has not attained (i. e., sexuality, husband, and children). According to this rough equation we expect the strongest reactions in young women still in the childbearing age and the mildest in older postclimacteric women with husbands and children. The degree varies inversely in the younger women according to whether they are married and have children. In the normal older women we anticipate that the chief problem will be adjustment to cancer and the possibility of death, whereas in the younger group it will be more of an immediate mixture of the two conflicts as previously outlined. We understand that there are many exceptions even within the so-called emotionally mature, normal group, and we offer this explanation only as a general "rule of thumb," not to be rigidly applied to every patient.

The neurotic woman, on the other hand, presents different problems—there has been a disturbance in the development of her sexuality. She is unable to accept her femininity completely or has strong doubts about her feminine abilities. Sexuality has become fused with guilt or hostility and thus has been rejected as a part of her "normal" functioning. Such a woman develops neurotic character patterns in order to solve this dilemma. She is masculine, frigid, or perhaps superficially sexual in an exaggerated fashion. In the former case she might develop attitudes of indifference or shame toward her breasts, whereas in the latter one might expect an excessive pride and overvaluation of the breasts.

Thus these women, through investing their breasts with irrational, disproportionate pride and shame, have made them the external focus for an internal conflict. A mutilating procedure involving this organ reawakens and intensifies the underlying neurosis.

In our series of cases the postmastectomy depressions were most extreme in women who had invested excessive feeling in their breasts. Underlying this reaction in these women was an exacerbation of their deeper neurotic conflicts. The surgeon should pay attention to such strong positive or negative breast complexes, and be alert for subsequent acute neurotic outbursts. It might be advisable to enlist the temporary assistance of a psychiatrist if he feels that such a reaction is liable to occur.

The physician's management is dependent on his constant awareness of these normal and abnormal breast reactions. In the preclimacteric and climacteric groups, he is particularly understanding of and sympathetic with the woman's feelings of danger and loss. He should not be too direct, hasty, or unfeeling in his approach. He must take time to discuss the problem thoroughly and to be an attentive listener. He sympathizes with her anxiety and dread over the prospect of losing the breast. He reveals his understanding of the emotional meaning and importance of the breast and clearly defines the necessity for the surgical step. The woman is not left with a feeling that the discussion was cold and mechanical. This enables her to view the surgeon as an understanding figure who regrets the urgent necessity for removal of the breast. Most important of all, it represents the beginning of a sound therapeutic relationship. The surgeon has been

known sometimes to disregard her feelings callously and thus to lose her therapeutic cooperation. She then views him only as an unfeeling technician who coldly takes from her an emotionally prized organ. One method of easing acceptance of amputation is to indoctrinate the woman preoperatively with the concept of her breast as a danger to her future. This causes a shift in thinking away from the breast as a prized possession toward viewing it as a foreign body that threatens life.

Any past feminine achievements—husband and children—should be introduced into the discussion to offset her sense of loss. The husband's aid has to be enlisted privately, so that he can be impressed with the importance of his role preoperatively and postoperatively. He should be instructed to be particularly tender, loving, and attentive during these phases. He should play up her other feminine charms through hospital gifts of clothes, cosmetics, and other items calculated to refocus her attention on still-present points for feminine pride. He should offer helpful sympathy, yet direct attention to the really important factor, that of the preservation of their relationship through the necessary medium of preserving her life by surgery. He should state clearly and repeat many times that the loss of the breast does not alter his love for her. We observed in many women that particular postoperative anxiety centered around a fear of the husband's rejection of her mutilated state. This developing anxiety can be aborted by the husband's prophylactic reassurance. Early in the postoperative phase the doctor should arrange for a woman to discuss prosthetics with the patient. Since people have become conditioned to advertising, it is well to borrow advertising techniques. A series of before and after pictures, with and without the breast prosthetic, is particularly helpful. Ideally this should be accomplished in the hospital, so that the woman can leave for home with the feeling that she is almost as intact physically as at the time of her admission. The woman's attention is thereby directed toward the goal of prompt healing. The husband is urged to express active interest in the state of the woman's operative wound. It must be stressed to him that he has to condition himself to accept the sight of the woman's nude body casually. He should treat it as part of their normal life. She thereby avoids the pitfall of concealing the chest from her husband. This concealment and denial of breast removal, because of the husband's imagined sensitivity, makes it impossible for her to accept the postoperative status of the body.

We do not mean to imply that the husband is supposed to enjoy the sight of the scar; obviously this is absurd. He should not, however, give his wife the impression that he never wants to see the scar. She is no more anxious to show it to him than he is to see it, but she has to have the feeling that he has accepted its presence and can, in the natural process of living together, view it without shock.

Some husbands have neurotic reactions to this viewing. These are the ones who deliberately avoid any sight of the operative incision and thus force their wife into a pattern of anxious concealment. Ideally each husband should be told in advance something of the difference between these possible normal and abnormal reactions

on his part. He should be impressed with the importance of his role in his wife's postoperative adjustment and the future of the marriage in general. His aid is enlisted in reporting to the surgeon any such strong continued pattern of avoidance within himself. He is made to understand that his normal reaction to the sight of the operative wound or incision will contain elements of shock, disappointment, anxiety, and sorrow. This is the same feeling that his wife will experience, and it is important that they share it together. Sharing her sorrow helps her to work through it more quickly. Crying on the part of the patient should be allowed. Do not try to stop it; it will make her feel better.

Furthermore, just as the husband must be warned regarding the normal and abnormal components of his feelings about her wound, so also the woman must be prepared to understand these reactions in her husband. A woman social worker can be of the utmost value in the management of many of these details and the ones already enumerated in regard to adjustment to mutilation of the breast.

The surgeon understands, therefore, that he is to anticipate more anxiety in women in the preclimacteric and climacteric periods and less in the postclimacteric woman as a reaction to the threatened breast amputation. If this ratio is reversed, he should realize that he is dealing with a neurotic patient. This should be a warning to him that he must be particularly careful in the management of such women. Ideally he makes an effort to evaluate the meaning and intensity of this reaction. He spends more time with them or perhaps calls a psychiatrist into consultation. Certainly he is alerted to the possibility that the postoperative emotional course will be a difficult one for the woman. This preoperative sensitivity will pay dividends in patient cooperation¹ and might well undercut or shorten a severe postoperative depressive reaction.

REACTION TO INVASION BY A POTENTIALLY DEADLY DISEASE

The problem of what and how much to tell the patient with breast cancer has almost as many answers as there are surgeons. Each doctor tends to work out a method according to his own feeling or lack of feeling about the problem. We believe that this results in hit-and-miss methods which often cause unnecessary emotional trauma to the patient. The common denominators in these miscellaneous approaches revolve around techniques of grave concealment or giving misleading partial information accompanied by an attempt at reassurance.

Every woman in our series immediately on discovering a lump in her breast or shortly thereafter associated it with cancer and the prospect of mutilation and possible death. Our cancer propaganda through the press, radio, films, and word of mouth has served its purpose. It is true that many of the women were afraid to face the reality implications of cancer of the breast and so put off seeing their physicians, but the fact remains that the idea of cancer was nonetheless firmly implanted within their minds. The woman with the breast lump, therefore, even

before she fearfully visits her doctor; has already anxiously confronted herself 100 times over with the word cancer. This is her frame of reference. The physician commonly confirms the lump and tells her that it is a tumor and that a biopsy will determine whether it is "serious" or "malignant." The latter word is used less often. Rarely is the term cancer used, and usually only if the patient does so. Even on such occasions the tendency is to ignore what she has said and to continue using vague terms. The woman rapidly stops "talking cancer" but never stops "thinking cancer." She reacts to the surgeon's avoidance of the word cancer as evidence of his feeling that the diagnosis is equivalent to a death sentence. This idea that the surgeon is also afraid of the disease increases her fear and serves as a confirmation of the un verbalized thought that she is doomed. Postoperatively, she may or may not be told the truth. Some surgeons are guided by whether or not the patient asks. Unfortunately, many patients do not ask. They believe it is cancer and feel that, since the surgeon does not talk about it spontaneously, the answer must be that he feels that they are going to die and does not wish to have to say so or to lie about it. They suffer in silence. By this time the husband has been informed of the diagnosis and, impressed with the surgeon's secrecy, may or may not tell his wife the truth. He gets the feeling that, if she were to be told, the surgeon would have done so. The woman senses from his forced attitude that something is radically wrong. She adds his evasiveness to the surgeon's silence as further evidence of impending doom. She too begins to play the game. She has been forced along with the others into the artificial role of actor. All playing the grim game of "It wasn't cancer. Everything is going to be all right. What a relief!" Usually she is left with the simple knowledge that she had cancer and probably still does; subsequently, when postoperative radiation is begun, she feels convinced.

This role of concealment on the part of the surgeon has the unfortunate consequence of removing him as a possible source of emotional aid. It also interferes seriously with the patient's cooperation in her postoperative treatment. She has a feeling of "What's the use?" and also of not completely trusting her doctor. The role of concealment on the part of the patient demands valuable energy for execution and represents an unnecessarily fatiguing and painful process.

Ideally, the surgeon should ask in the very beginning of the first interview, during the history taking and before the physical examination, whether or not the patient has been worried about the possibility of cancer. This touches on a common problem and at least brings the fear out into the open. The patient then finds it easier to relate herself to the physician and ventilate some of her anxiety. They should be prepared for biopsy and potential mastectomy. This preparation consists of a careful, considerate discussion of the biopsy and the chances of mastectomy. The possibility of radical surgery should not be underplayed, since it is to the patient's advantage to be warned and to have the brief preoperative period in which to begin adjustment to the prospect of cancer and mutilation. Too often the patient with cancer of the

1. Cockerill, E. E.: The Patient Has Cancer, *Pub. Health Nursing* 35: 552-558 (Oct.) 1943.

breast is misled and then awakens with the shocking realization of amputation. This undermines her confidence in the surgeon and generates hostility, which interferes with their future relationship.

Some surgeons have said: "Talk about cancer! I'd have to lock the windows first." This attitude reflects a deep and chronic anxiety on the surgeon's part regarding his ability to handle the patient's emotional reaction to cancer. It is obviously predicated on his irrational belief that cancer of the breast is fatal and that the woman would kill herself because of the knowledge. A person trapped on a high cliff by a charging lion might well leap to death as an alternative to a hopeless and painful situation. But suppose that person is reminded that he has a highpowered rifle in his hands. Who is going to commit suicide with a 50-50 chance of survival? The rifles in our case are facts about modern therapeutic techniques and the resulting prognosis. It is possible, of course, that a severely neurotic person might utilize this irrationally as reason for a suicidal attempt. Suicide could also be precipitated by threatened loss of a job or a love partner, or by a change in the weather. It is necessary, therefore, for the surgeon to examine his patient's emotional reactions during the physical examination and history taking. It doesn't take a skilled psychiatrist to spot a badly disorganized person or one who is already severely depressed. Such a patient must be handled more cautiously and dealt with only when the surgeon feels certain about the degree of the neurosis. Psychiatric consultation would be most helpful. The important point is that the average woman with cancer of the breast should not be allowed to suffer from emotional mismanagement because of the potential reaction of a rare seriously disorganized patient with the same illness.

We believe that this generalized, undifferentiated "kid gloves" attitude on the part of the surgeon stems from genuine anxiety over the welfare of the patient. It represents an outdated attitude, a carry-over from the real problems that confronted the physician of several generations ago. Cancer of the breast then equaled death—there was no alternative. This concept has been handed down from generation to generation as an essential piece of bedside technique. The conditions that created the attitude have ceased to exist; yet we automatically continue the attitude. This results in communicating to our patients the feeling that the conditions must also still exist.

Approximately 17,000 women die in the United States each year of cancer of the breast. There are about 70,000 cases under observation in the United States at any given time. The highest incidence of breast cancer is between the ages of 40 and 50, about 75% occurring after the age of 40. There is an increasing susceptibility with advancing years. There is some evidence to indicate that mammary cancer is commoner in single than in married women and also that among married women with mammary cancer there is a lower percentage who have borne children or who have nursed them. This disease is commoner among women who have or who have had benign epithelial tumors. Cancer of the breast is commoner in women with a family history of the disease. The average duration of life is four years.

The prognosis is definitely poorer in women under 40 and especially under 30 years of age. Pregnancy and lactation exert an unfavorable influence.

The extent of the disease when treatment is begun is the most important factor influencing prognosis. Both the incidence and the number of deaths from mammary cancer seem to be increasing. Between 30 and 35% of patients survive five years after radical surgery, the curability being about 80% when the disease is confined to the breast and about 40% when the axillary nodes are invaded. Radical mastectomy followed by postoperative radiation in selected cases is the generally accepted procedure for presumably operable cases.

In our study every woman seen by the psychiatrist was told by the interviewer that he did not know whether she had originally come to the Tumor Institute because of cancer of the breast. He knew only that she had some disease of the breast, and he was interested in talking with her about her reaction to it. The word cancer was freely used by the interviewer throughout the sessions. The responses elicited were dramatic: A few women were so relieved to hear someone say cancer that, like children with a new word, they said it again and again. All appeared to accept it with relief. About half were found to be living in a world in which people around them studiously avoided using the word cancer. All were asked if they had inquired of their surgeon as to whether they had cancer, and if they had not, why not. For the most part, those who had failed to ask had interpreted the surgeon's silence as has been previously outlined. A recent statistical study by Kelly and Friesen² showed that 89 of 100 patients with cancer of various organs and 729 of 740 patients over 45 years of age undergoing yearly examinations in an effort to detect cancer in an early stage wanted to be told of the presence of cancer.

All the women with cancer of the breast sooner or later reacted with anxiety over possible death. This is a normal reaction. Some of them were able to verbalize it, some repressed it completely, and some carried it unspoken, allowing themselves to be paralyzed with the growing and never quiet fear. The development of anxiety in the patient with breast cancer is a normal concomitant of the disease. It should be anticipated, looked for, and utilized therapeutically. Failure to express anxiety should be viewed with alert suspicion. Everyone involved in a situation with a threat to life reacts with anxiety. This is the mind's way of alerting the self to danger. It is a signal that warns one to prepare for an emergency. The woman with the integrated ego appraises the situation objectively, considers all the facts at hand—involving past performance, degree of immediate danger, and alternative plans for meeting the threat—and then selects a plan that is the most realistic and provides the best chance for survival. This process requires a degree of anxiety that serves as a stimulant for preparation. Too much anxiety will paralyze planning and result in uncoordinated, unrealistic behavior. It should be the goal of every surgeon to keep this anxiety within optimal limits. He partially achieves this by helping the patient

2. Kelly, W. D., and Friesen, S. R.: Do Cancer Patients Want to be Told? *Surgery* 27:822-826 (June) 1950.

with the process of planning. This involves acquainting the patient with the realistic facts concerning cancer in general, her cancer, biopsy, convalescence, postoperative treatment, and prognosis. She is much better equipped to handle calmly delivered clinical data than the conglomeration of old wives' tales, misinformation, and distorted fantasies about cancer which immediately crowd forth into her mind at the discovery of the lump.

UTILIZATION OF ENERGY TO COMBAT DISEASE

Why is it important to prevent the occurrence of excessive emotional conflicts over cancer of the breast and subsequent mastectomy? In order to answer this we must say a little about the nature of human energy. Every person according to his or her individual constitution has a limited amount of energy available for the work of the body and the mind. Under conditions of physical health, a certain basic amount is utilized in the work of anabolism and catabolism. Above this is the quantity devoted to the problems of successful adaptation to the external environment. This involves the effort expended in socioeconomic endeavors and interpersonal relationships. The neurotic suffers through binding of varying amounts of energy that would otherwise be available to those two essential tasks, i. e., physiological and psychological functioning. The energy is bound by the constant necessity to control strong antisocial impulses or to struggle with unresolved neurotic conflicts. The resolution of an emotional symptom in psychoanalysis results in fresh bursts of enthusiasm or productivity on the part of the patient. This is an expression of energy freed from its static work of struggling with the previously existing neurotic conflict. In unusual physiological or psychological states, i. e., organic disease or an acute problem of environmental adjustment, the balance of available energy shifts to the area which requires it most.

A diseased person naturally cuts down on his external activities and concentrates attention and the freed energy on the work of combating the disease process. It is only as he is on the road to recovery that interest shifts from the body back to the world outside.

We know that the body has resources for combating attack by disease. The problem is to make ideal conditions available to the body in its work of defense and recuperation. Little is known about the defensive resources of the body against cancer, but, according to its reaction to other disease processes, it appears that the same reaction must occur in the cancer patient. Perhaps it is on this basis that we eventually will explain occasional "miraculous cures," or how patients live far beyond the predicted life span. True, the resistance against cancer usually is not enough by itself, but aided by surgical and radiological methods it becomes a more potent force and one to be encouraged. The cancer patient should be acquainted with this idea, so that she is given a feeling that there is something within her that, aided by the surgeon, can fight the cancer. This gives a sense of active participation and removes the uncomfortable feeling that she is defenseless against the cancerous invader. Her total available energy should be mobilized for dedication to this task. It would be unfortunate were she to maintain the previously outlined

ostrich-like effort to deny cancer. Here she would be squandering valuable energy in her superficial and fatiguing work of concealment and acting, in addition, to the energy expended in her anxiety about inevitable death. We believe that part of the weight loss in cancer is often related to this very concept, i. e., denervating, concealed worry and anxiety over her doomed status.³

Energy conservation is an old and simple concept. It has long been applied by physicians through their intuitive efforts to free the suffering person's mind of troubling environmental problems. The way of expressing it has been: "Don't let that bother you. Just concentrate on getting better."

This is the chief underlying rationale of being humanly factual with the patient with cancer of the breast. Acquaint her with the encouraging details of her prognosis and with her role in the total treatment. Explain all the necessary therapeutic steps, such as biopsy, mastectomy, and radiation, and why they are important. Pay attention to the status of her emotional health, do not allow her to build up and retain unnecessary fears and feelings of inevitable death. Explain the need for entering into the next six months prepared for total battle. When the patient fails to mobilize her defenses, as reflected in acute emotional reactions or in putting off treatment hours, bring it to her attention and discuss the reason. Should she fail to respond, do not hesitate to call in a psychiatrist for the job of channeling energy back into the work of disease resistance and medical cooperation.

We do not advocate this approach for cancer in general, only cancer of the breast. Patients with other types of cancer present different reality problems and their anxiety is based on different psychological threats related to the deep emotional meaning of the organ involved.

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3. Rosenbaum, M.: Personal communication to the authors.

Food Refusal in Children.—Any of us can say what the average weight is for a child of a given age and sex, but none of us can say what the normal is, for it is impossible to define the normal. Many parents and doctors are obsessed with weight charts, and think that any departure from the figures given by them means that there is something wrong with the child. A child may be pounds below the average in weight and yet be perfectly normal. . . . Many books give diet sheets for normal children, laying down rigid quantities of foods even for a two-or-three-year old child. Such books inevitably cause trouble, for mothers try to force their children to eat the quantities laid down, and then food is refused. . . . By far the commonest cause of food refusal is food-forcing. Practically every case of poor appetite in children who are free from organic disease is due to this. . . . It would be surprising if nature had failed to equip human beings with an appetite sufficient for their needs, and yet had remembered lambs, calves and other animals, for one does not see animals having to be forced to take their food. . . . The absolute essential in treatment is to stop all forcing. There must be no coaxing, no persuading, no anxious looks at the plate, no bribing, no forcing, no threatening and no punishment. . . . The child is offered the food in a matter of fact take it or leave it manner, and if he takes it no comment is made. There is no need to praise him for it any more than he is praised for playing with his toys. If he refuses it no comment is made.—R. S. Illingworth, M.D., *Food Refusal in Children*, *Journal of the Royal Institute of Public Health and Hygiene*, December, 1951.

USE OF BISHYDROXYCOUMARIN (DICUMAROL®) IN THE PRESENCE OF IMPAIRED RENAL FUNCTION

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and

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The concept that impaired renal function is a contraindication to bishydroxycoumarin (dicumarol®) therapy had its origin in early animal experiments. Bollman and Preston¹ produced renal damage in dogs by subcutaneous injection of uranium acetate or by bilateral ligation of the ureters and found a marked sensitivity to bishydroxycoumarin. They noted a similar effect after bilateral nephrectomy. Richards and Steggerda² found

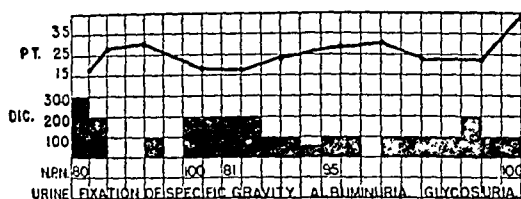


Chart 1 (case 1).—Data on patient with intercapillary glomerulosclerosis in uremia and thromboembolism. In this and the following charts the squares represent time in days. The prothrombin time (P. T.), in seconds and the dosages of bishydroxycoumarin (DIC), in milligrams, as well as the nonprotein nitrogen level, in milligrams per 100 cc., and other renal data are shown.

that bilateral nephrectomy in rats greatly increased the effect of bishydroxycoumarin. An early clinical report by Allen, Barker, and Waugh³ stated that the effect of bishydroxycoumarin on prothrombin time is excessive in cases of renal insufficiency and advised that the drug be used very cautiously or not at all in these patients. Allen, Barker, and Hines⁴ cited cases of two patients treated with this drug, in whom suppression of urine developed owing to the accumulation of crystals of sulfonamide compounds in the renal pelvis. The prothrombin time, which was increased in association with the anuria, returned to normal when urine again was excreted by the kidneys.

Overman and associates⁵ were unable to detect bishydroxycoumarin in the urine of dogs after administration of large amounts. This finding, along with their own animal experiments cited above, suggested to Bollman and Preston¹ that the kidney plays an important role

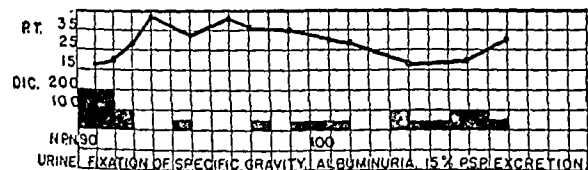


Chart 2 (case 2).—Data on patient with chronic diffuse glomerulonephritis in uremia.

in the destruction of this compound. Weiner and colleagues,⁶ in studies on man, found only traces of the drug in the urine after its administration and concluded that it is almost completely metabolized in the body. In a group of patients showing hemorrhagic manifestations of bishydroxycoumarin toxicity, Wright and Prandoni⁷ found none with renal dysfunction, although studies

were carried out with this in mind. Shapiro and Weiner⁸ state that the evidence for considering renal disease a contraindication to bishydroxycoumarin therapy is inconclusive.

In 1949 we were confronted with a patient who had thromboembolic disease and impairment of renal function. Since heparin is excreted by the kidney,⁹ and patients with renal disease are sensitive to heparin,¹⁰ we decided to treat this patient with bishydroxycoumarin. It was found that the patient (Case 1) was resistant to the drug, for a high dosage was required to maintain a therapeutic prothrombin time. The drug was subsequently given to eight other patients with impaired renal function, and the findings form the basis of this report.

METHOD

Patients with varying degrees of impairment of renal function were selected for the study. Patients with associated liver disease, gross hematuria, bleeding from the gastrointestinal tract, or

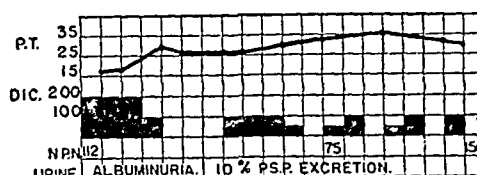


Chart 3 (case 3).—Data on patient with nephrosclerosis in uremia.

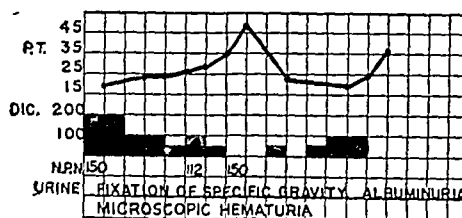


Chart 4 (case 4).—Data on patient with chronic diffuse glomerulonephritis in uremia.

nausea or vomiting caused by uremia were excluded. The Link-Shapiro¹¹ modification¹² of the Quick method was used in making the prothrombin time determinations, which were done

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1. Bollman, J. L., and Preston, F. W.: The Effects of Experimental Administration of Dicumarin; 3,3'-Methylene-bis-(4-hydroxycoumarin), *J. A. M. A.* 120: 1021 (Nov. 28) 1942.

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3. Allen, E. V.; Barker, N. W., and Waugh, J. M.: A Preparation from Spoiled Sweet Clover (3,3'-Methylene-bis-(4-hydroxycoumarin)) Which Prolongs Coagulation and Prothrombin Time of the Blood: A Clinical Study, *J. A. M. A.* 120: 1009 (Nov. 28) 1942.

4. Allen, E. V.; Barker, N. W., and Hines, E. A., Jr.: *Peripheral Vascular Diseases*, Philadelphia, W. B. Saunders Company, 1946.

5. Overman, R. S.; Stahmann, M. A.; Sullivan, W. R.; Huebner, C. F.; Campbell, H. A., and Link, K. P.: Studies on the Hemorrhagic Sweet Clover Disease: VII. The Effect of 3,3'-Methylenebis(4-hydroxycoumarin) on the Prothrombin Time of the Plasma of Various Animals, *J. Biol. Chem.* 142: 941 (Feb.) 1942.

6. Weiner, M.; Axelrod, J.; Shapiro, S., and Brodie, B. B.: Fate of Dicumarol in Man, *Federation Proc.* 8: 345 (March) 1949.

at least three times each week. In some cases, as shown in Charts 2 to 7, the determinations were made more frequently. Bishydroxycoumarin was given orally in doses to reach and maintain prothrombin times ranging from 25 to 50 seconds (30% and 10%), which are considered the optimal levels for therapy of thromboembolic disease.

DATA

The prothrombin times and bishydroxycoumarin (dicumarol®) dosages for the nine patients are summarized in Charts 1 to 9. The clinical diagnoses and pertinent renal data are included. Case 1 was that of a 54-year-old woman. Case 2 was that of a man aged 63. Case 3 was that of a 67-year-old woman. Cases 4 and 5 were those of men, aged 53 and 68. Cases 6, 7, 8, and 9 were those of women, aged 35, 43, 55, and 62, respectively. Only one of the patients (Case 8) was sensitive to the drug. Vitamin K was required to return the prothrombin time to a normal level. This patient was the only one in whom uremia progressed, and a second course of bishydroxycoumarin therapy was reinstituted for comparative study six days before death. At this time, when the nonprotein nitrogen level was 129 mg. per 100 cc., a dose of 600 mg. administered over a three-day period delayed the prothrombin time to 30 seconds; whereas previously, when the nonprotein nitrogen level was 47 mg. per 100 cc., a dose of 550 mg. given over a three-day period produced a prothrombin time

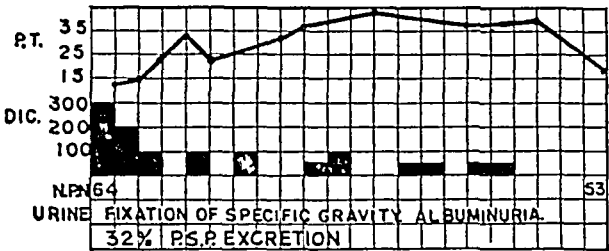


Chart 5 (case 5).—Data on patient with nephrosclerosis in uremia.

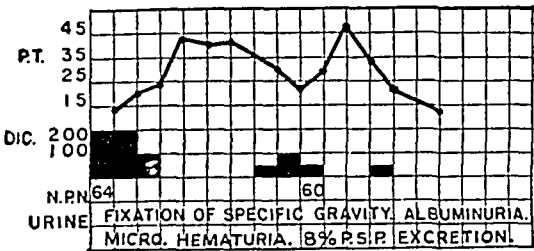


Chart 6 (case 6).—Data on patient with chronic diffuse glomerulonephritis in uremia.

of 57 seconds. It would seem that neither sensitivity nor resistance to the drug are related to the degree of azotemia. The remaining patients (except Case 9) showed varying degrees of uremia, without sensitivity to the drug, and required the usual dosages for maintenance. The patient in Case 9, the only patient without uremia, had marked impairment of renal function, as was

evidenced by an inulin clearance of 60 cc. per minute (normal 117 ± 15.6) and an effective renal plasma flow of 218 cc. per minute (normal 594 ± 102.4). This patient was not sensitive to bishydroxycoumarin. Two patients (Cases 4 and 6) showed microscopic hematuria before and during the period of treatment, without any increase in renal bleeding. None of the patients

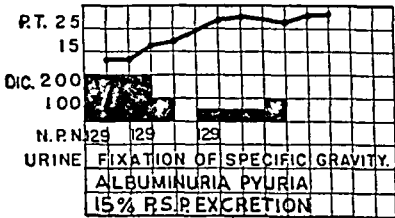


Chart 7 (case 7).—Data on patient with chronic pyelonephritis in uremia.

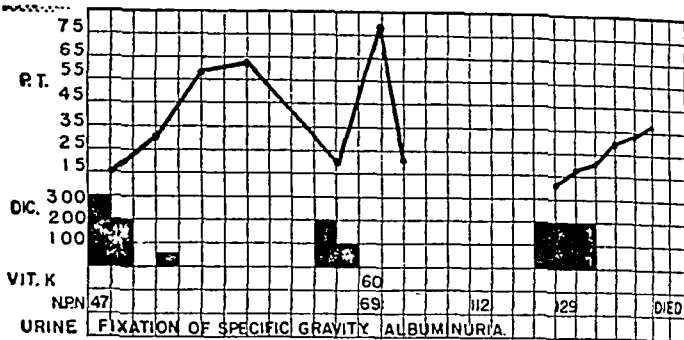


Chart 8 (case 8).—Data on patient with chronic diffuse glomerulonephritis in progressive uremia. Because the patient was sensitive to bishydroxycoumarin, vitamin K (shown in milligrams) was required to return the prothrombin time to a normal level.

had hemorrhagic complications from bishydroxycoumarin therapy. No beneficial or untoward effect on the course of the underlying renal disease was noted during the relatively short period of administration.

COMMENT

The data presented indicate that bishydroxycoumarin therapy may be used safely in patients with chronic renal insufficiency. This observation becomes of practical clinical importance when there is need for anticoagulant therapy in these patients. Since heparin is poorly tolerated by patients with renal disease, bishydroxycoumarin is the drug of choice. The conclusions reached as a result of animal experiments may not be applicable to chronic renal disease in man, since in all these experiments the kidneys were completely functionless. Furthermore, in the experiments of Bollman and Preston¹ uranium may have exerted a toxic effect on the liver¹³ as well as on the kidney. The two cases of Allen, Barker, and Hines⁴

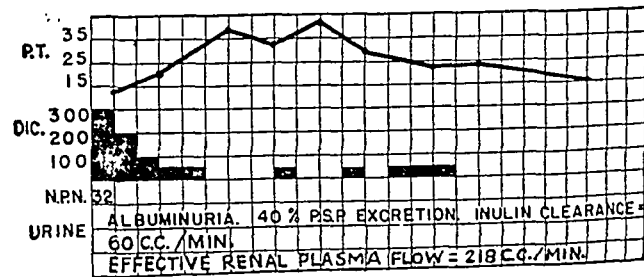


Chart 9 (case 9).—Data on patient with chronic diffuse glomerulonephritis.

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10. Sachs, J. J.: Unpublished data.
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12. The thromboplastin was furnished by Chilcott Laboratories Division of the Maltine Company.
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were likewise acute cases of complete renal failure, suggesting that the response to bishydroxycoumarin in patients with anuria is different from that in patients with chronic renal insufficiency without anuria. The reason for this difference is not clear.

SUMMARY

Bishydroxycoumarin (dicumarol®) in usual dosage was given to nine patients who had chronic renal disease and impaired renal function, without producing unusual effects on the prothrombin time. Chronic renal insuff-

iciency does not seem to be a contraindication to anticoagulant therapy with bishydroxycoumarin, provided there is no bleeding in the gastrointestinal tract or gross blood in the urine.

99 Pratt St., Hartford 3 (Dr. Sachs).

LUMBAR PUNCTURE HEADACHE

Daniel Sciarra, M.D.

and

Sidney Carter, M.D., New York

The occurrence of undesirable reactions following lumbar puncture is not uncommon. The incidence has been variously reported as ranging between 5 and 75%.¹ A prominent feature of the postlumbar puncture reaction, and often its only manifestation, is headache. This symptom usually appears 12 to 24 hours after the puncture, though it may occur in a few hours or may be delayed for several days. Characteristically, the headache is relieved when the patient lies down and becomes accentuated when the patient either sits or stands. In most cases the headache persists for several days, but occasionally it may last for as long as eight weeks.

Various explanations have been given for the appearance of the headache, and various factors have been noted that will modify or prevent it. Some observers have felt that postlumbar puncture headache is psychogenic² and that its incidence is greater in persons known to be neurotic.³ Other investigators, dealing primarily with psychiatric patients, have stated that the incidence of postlumbar puncture headache is not dependent upon the emotional stability of the patient.^{1a} The more widely accepted view at present is that the headache is of mechanical origin. Among the mechanical factors that have been considered as contributing to the occurrence of headache are the size of the needle, the position of the patient, and the quantity of fluid removed. It has been known for many years that the size of the needle is a factor in the occurrence of headache; in general, the use of a small-bore needle is attended with a lower incidence of postpuncture headache.⁴

The value of bed rest immediately after the puncture in preventing the occurrence of headache has been investigated by many observers. For the most part they have concluded that the position of the patient after the puncture does not play a significant role in the occurrence of headache.⁵ However, in most of these series the patients were kept in bed less than 24 hours. Since the headache can occur up to several days after the puncture, the period of bed rest that has usually been tried does not appear to be adequate.

Not infrequently in clinical practice a small amount of fluid is removed in the hope that this will prevent the appearance of a postlumbar puncture headache. There is some evidence to indicate that the amount of fluid⁶ removed has no direct relationship to the occurrence of headache.⁷ MacRobert⁸ in 1918 first postulated that the probable cause of lumbar puncture headache was the

hole in the dura made at the time of puncture. This would help explain why postlumbar puncture headache is worse when the patient is sitting up and disappears when he is lying flat, why the incidence of headache is less when only a small dural opening is made, and why the quantity of fluid removed makes little or no difference in the occurrence of headache. If it is true that the occurrence of headache is dependent upon the hole in the dura and not upon the quantity of fluid removed, it would seem that the incidence of headache should be as great among patients who simply have a dural puncture without removal of fluid as among those who have a puncture with the removal of fluid. We have recently had occasion to do a clinical experiment that has some bearing on this point.

METHOD

Lumbar punctures were performed in a group of patients who were studied on a neurological service. These patients were all ambulatory and had no complaint of headache. In all cases the lumbar puncture was done with the patient in a horizontal position. A no. 18 needle was used in every case. The patients were divided into two groups. In one group (62 cases) a routine lumbar puncture was done with the removal of 10 to 12 cc. of cerebrospinal fluid; in the second group (45 cases) a similar puncture was done, but after the dura was pierced and cerebrospinal fluid had appeared in the needle, the needle was withdrawn. All the patients were allowed up immediately after the puncture and were instructed to follow their usual routine. Since no special instructions were given the patients, the presence of a headache became

From the Department of Neurology, Columbia University, and the Neurological Institute, Presbyterian Hospital.

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apparent in one of two ways. It was either called to the physician's attention or its occurrence was ascertained by a routine check of each patient one week after the puncture.

RESULTS

Lumbar punctures were made in a total of 102 cases. In 45 of the 102 patients a lumbar puncture was performed, but no fluid was removed. In this group, a postlumbar puncture headache developed in 17 patients (38%). In 15 patients the headache developed within the first 24 hours after the puncture, in one it began in 48 hours, and in another in 72 hours. Thus in 88% of those in whom a headache developed, the onset was within the first 24 hours. In the patients in whom headaches developed without removal of fluid, the duration of the headache was variable. In none of the cases did the headache last less than two days, in one case it was present for two days, but in the majority of the cases (94%) it persisted for three to five days.

In 62 of the 102 cases a routine lumbar puncture was done with the removal of 10 to 12 cc. of cerebrospinal fluid. In 29 out of the 62 cases (46%) a postlumbar puncture headache developed. In 26 patients the onset of headache was within the first 24 hours after puncture. In two patients the headache appeared 48 hours after the spinal tap, and in only one patient was its appearance delayed for 72 hours. Therefore, in 90% of those with headache, the headache appeared within the first 24 hours. In this group the duration of the headache was carefully tabulated in only 16 cases. The headache in these cases lasted from one to four days. Only one patient had a headache that lasted for one day, while in the rest of the cases (94%) the headache persisted for two to four days.

COMMENT

These observations indicate that the removal of cerebrospinal fluid does not play a significant part in the production of postlumbar puncture headache. Cook⁷ compared the incidence of postlumbar puncture headache in groups of patients from whom he removed varying amounts of fluid. Essentially he concluded that the amount of fluid removed had no influence on the occurrence of headache. It could therefore be postulated that one of the primary mechanisms in the production of postlumbar puncture headache is the leakage of cerebrospinal fluid through the hole in the dura made by the lumbar puncture needle. This theory was initially advanced by MacRobert⁸ and amply supported by many other investigators. Fluid has been seen to leak from a persisting hole in the dura both at laminectomy⁹ and at autopsy.¹⁰

Indirect evidence in support of the leakage theory has been supplied by numerous observers,¹¹ who have noted a marked drop in cerebrospinal fluid pressure at the time of a second lumbar puncture. This drop tends to occur within the first 24 hours and tends to be commoner in the patients in whom postlumbar puncture headache develops.¹²

If the presence of a hole in the dura is a factor in the production of postlumbar puncture headache, then the size of the hole may also influence the occurrence of headache. There is a great deal of evidence to indicate

that this is true. Many investigators have observed that with the use of a small-bore needle the incidence of postlumbar puncture headache is markedly reduced.¹³

SUMMARY AND CONCLUSIONS

Lumbar punctures were done in 102 patients. In the 62 patients from whom cerebrospinal fluid was removed the incidence of postlumbar puncture headache was 46%. The majority of these headaches came on within 24 hours after the lumbar puncture and lasted 2 to 4 days. In the 45 patients in whom the dura was pierced but from whom no fluid was removed, the incidence of postlumbar puncture headache was comparable (38%). In this group the headache also came on within the first 24 hours and lasted 2 to 5 days.

It is concluded that the amount of cerebrospinal fluid removed at the time of puncture up to 12 cc. has no effect on the frequency of occurrence of postlumbar puncture headache. This may have immediate clinical applications. The physician who does a lumbar puncture may often be faced by at least two problems. One is the obtaining of sufficient fluid on which to do necessary studies and the other is the avoidance of postlumbar puncture headache. Since 10 to 12 cc. of cerebrospinal fluid is usually sufficient for routine studies and since the removal of lesser amounts does not decrease the incidence of headache, it is suggested that at least 10 cc. be removed routinely.

710 W. 168th St. (Dr. Sciarra).

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12. Footnote 11b, d, and f.

13. Footnotes 1a, 4, 5, 11d, and 11f.

Transmission of Poliomyelitis.—Available knowledge justifies the conclusion that human feces derived from patients and healthy carriers is the most significant source of virus in nature. Available evidence indicates that the virus which is occasionally present in the throat of patients and healthy carriers does not ordinarily reach the outer environment in significant amounts by droplets from the mouth or nose. . . . The period of communicability cannot at present be said to be limited to a few days before and a few days after onset of illness, but should rather be regarded as potential during the period that virus is generally eliminated in the feces. . . . One may use as a guide the fact that approximately 50% of patients still have demonstrable virus in their stools three to four weeks after onset. . . . Excepting artificial conditions, entry of poliomyelitis virus by way of the mouth can be justifiably regarded as the usual mode of infection. Accordingly, it follows that contaminated food and drink are as important as contaminated fingers in introducing the virus into the body. . . . Under certain conditions, in urban as well as rural communities, filth flies as well as human beings can be carriers of poliomyelitis virus, and should be regarded in the same light.—Albert B. Sabin, M.D., *Transmission of Poliomyelitis Virus, The Journal of Pediatrics*, November, 1951.

CLINICAL NOTES

PRIMARY TREATMENT OF CERVICAL CARCINOMA WITH "KREBIOZEN"

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and

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The following case report constitutes one of a series in which varied malignant growths were treated with "krebiozen" to evaluate the effect of the drug. Since the drug allegedly had been standardized in vivo on the basis of beneficial influence on an untreated mammary carcinoma, it was felt that an untreated, relatively early, cervical malignant growth would offer a unique opportunity to observe any regression produced by the medication alone.

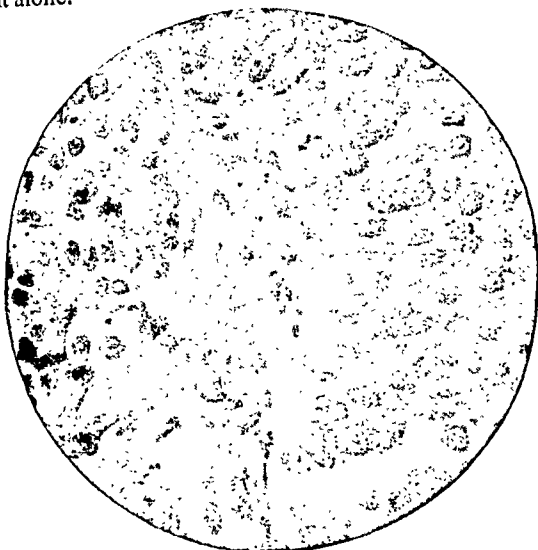


Fig. 1.—Transitional cell carcinoma.

REPORT OF A CASE

Mrs. A. J., a white woman, 56, was admitted to Mercy Hospital Institute of Radiation Therapy on June 5, 1951, complaining of vaginal discharge and bleeding since October, 1950. She had had an uneventful menopause in 1947 and had been in good health until the onset of her present symptoms. Her previous medical and surgical history was noncontributory. She had been delivered uneventfully of her only pregnancy 35 years previously.

Her initial physical examination findings were not remarkable except for a blood pressure of 142/90 and the following pelvic findings: a second degree cystocele and a uterus in first degree retroflexion, smooth, movable, and with minimal enlargement. The adnexa were essentially normal. The cervix revealed a proliferating lesion at 5 o'clock, which bled readily on contact; the growth extended partially around the cervical os on the left with beginning extension into the left paracervical areas. The clinical impression was carcinoma of the cervix uteri, Group 3. Microscopic diagnosis of the biopsy specimen taken that day was reported as transitional cell carcinoma (Fig. 1).

Clinical Course.—On June 11, 1951, the patient was admitted to the hospital for laboratory evaluation of renal function. The pertinent findings were: a red blood cell count of 4,300,000, a hemoglobin of 87.7%, a nonprotein nitrogen of 35 mg. per 100 cc., a urea nitrogen of 9 mg. per 100 cc., and a urea clearance of 42.7%.

On June 12, 1951, the first dose (1 cc. [0.01 mg.]) of "krebiozen" (batch number S3 A7 T4) was given. On June 15, 1951, the second dose (1 cc. [0.01 mg.]) of "krebiozen" was given. On July 9, 1951, examination revealed no change in the appearance or extent of the lesion. On July 10, 1951, and July 13, 1951, the third and fourth doses of "krebiozen" were administered. Ex-

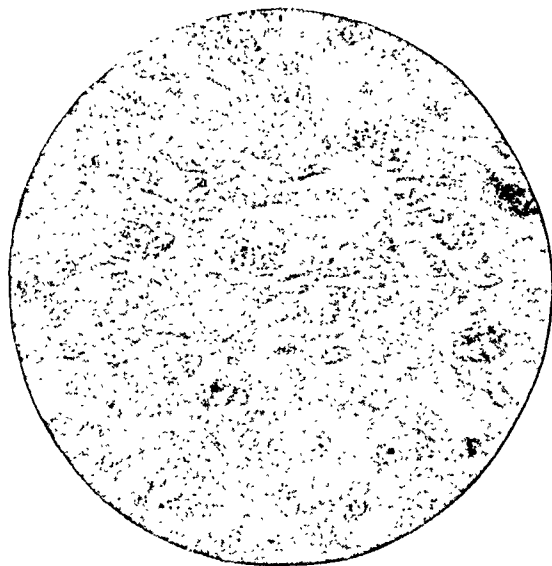


Fig. 2.—Photomicrograph showing no intrinsic cellular change after course of "krebiozen."

aminations on July 20, August 3, August 10, September 1, and September 15 revealed no regression of growth. A photomicrograph (Fig. 2) showed no intrinsic cellular change.

On Sept. 24, 1951, a total abdominal hysterectomy, bilateral salpingo-oophorectomy and pelvic lymphadenectomy were done. At the time of operation the upper part of the abdomen was examined, and the liver was found to be smooth; the gallbladder, stomach, and kidneys were normal. The uterus was

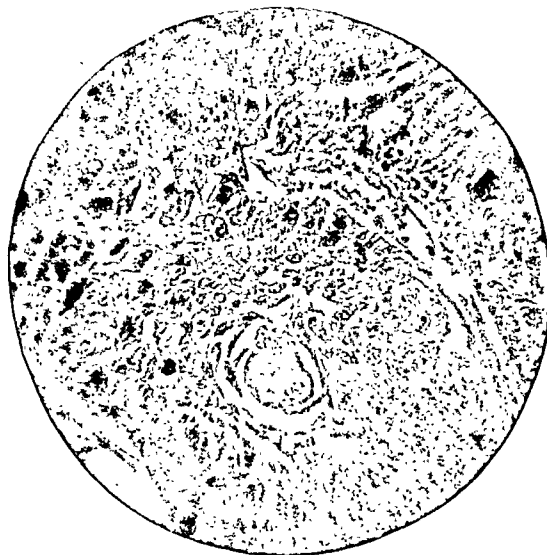


Fig. 3.—Photomicrograph showing infiltrating carcinoma with pearl formation.

small, freely movable, and in an anterior position. Both tubes and ovaries appeared normal. On opening the leaves of the broad ligament, on the left side, the iliac vessels were found to be covered by a large amount of fatty tissue. At the junction of the left internal and external iliacs with the common iliac, several lymph nodes were found that were hard and seemed to be infiltrated with carcinoma. This was the only area found during the entire operation that seemed to be invaded with carcinoma.

Pathological study of the tissues removed revealed that the cervix was infiltrated by a soft pinkish-gray tumor, which involved both cervical lips and a large portion of the cervical canal. The entire growth measured about 2 by 3 cm. The peritoneal surface of the uterus showed no significant changes. The uterine cavity was normal in size and lined with an atrophic endometrium. The fallopian tubes showed no significant changes. The ovaries were normal in size, olive shaped, and each measured about 35 × 25 × 15 mm. The tissues removed from the left iliac area consisted of indurated fat and two whitish-gray, rather firm masses, the largest of which was about 2 cm. long. Both appeared to be lymph nodes. The specimen removed from the right iliac area consisted of dark-brown soft tissue mixed with a large amount of fat. The tissues removed from the obturator area consisted of soft lobulated fat containing whitish-gray granular well-formed nodes, the largest one being 10 mm. in diameter. Microscopic examination of the cervix revealed an infiltrating carcinoma with areas of necrosis and hemorrhage. There were occasional pearl formations and numerous mitotic figures. Sections from the uterus showed atrophic changes of the endometrium. The myometrium showed areas of beginning fibrosis and was infiltrated with thickened blood vessels. Sections from the ovaries revealed atrophic changes. Microscopic examination of all lymph nodes removed revealed proliferation of the reticuloendothelium and occasional areas of hemorrhage, but no tumor cells were found.

Microscopic diagnosis was reported as follows: infiltrating carcinoma of the cervix, atrophic changes of the endometrium and ovaries, and reticuloendothelial proliferation of lymph nodes (Fig. 3).

Two follow-up examinations have revealed the pelvis to be free of recurrence to date.

CONCLUSION

There was no evidence that "krebiozen" had any curative or destructive effect on the lesion in this case.

55 E. Washington St. (Dr. Schmitz).

ENHANCED CLINICAL EFFECTIVENESS OF PURIFIED CORTICOTROPIN

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I. N. Rosenberg, M.D.
V. W. Westermeyer, M.D.
and
E. B. Astwood, M.D., Boston

Earlier clinical experience with partially purified corticotropin indicated that the purified preparation was somewhat more effective therapeutically than a standard preparation in equivalent amounts.¹ The material, which had been purified using cellulose,² assayed 20 U. S. P. units per milligram by the Sayers rat test³ but was judged

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Dr. David Klein of the Wilson Laboratories supplied the gelatin preparation of purified corticotropin in the form of corticotropin (Wilson) gel.
This investigation was supported, in part, by research grants from the National Institutes of Health, United States Public Health Service, and from the American Cyanamid Company. Dr. V. W. Westermeyer is a Fellow of the New England Chapter, Arthritis and Rheumatism Foundation.
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to have a clinical potency of 30 units per milligram. Subsequent improvement in the method used in this laboratory for purification of corticotropin⁴ has permitted clinical use of a considerably more potent preparation. The purified corticotropin that was obtained in good yield using oxycellulose contained 80 units per milligram by

TABLE 1.—Dose Requirement of Aqueous Purified Corticotropin Administered Every Eight Hours

Disease	No. Patients	Dose Controlling Disease	
		U. S. P. Units/Day	Mg./Day
Rheumatoid arthritis.....	2	15	0.19
	3	30	0.375
	2	48	0.6
	4	60	0.75
	1	120	1.5
Ulcerative colitis.....	1	60	0.75
Asthma	2	40	0.5
	1	60	0.75
Acquired hemolytic anemia..	1	60	0.75
Boeck's sarcoid.....	1	60	0.75

bioassay. The clinical effectiveness of an aqueous solution, as judged from the dose requirements in 18 patients (table 1), suggested the therapeutic potency was about 150 units per milligram. The average daily dose was 0.6 mg. (48 units).

Purified corticotropin was administered by subcutaneous injection and was given every 8 hours in aqueous solution, or every 24 or 48 hours in a gelatin solution, or as a suspension in sesame oil. The relative effectiveness of the preparations often was compared in the same patients. Both gelatin and oil prolonged the action of corticotropin, but gelatin was more efficient and reduced the daily dose below that required with injections of the aqueous solution at eight hour intervals (tables 1 and 2). Evidence of excessive dosage was common in this series of patients, particularly before the augmented clinical potency was appreciated. Hirsutism, rounding of the

TABLE 2.—Dose Requirement of Long-Acting Preparations of Purified Corticotropin Administered Every Twenty-Four to Forty-Eight Hours

Disease	No. Patients	Vehicle	Dose Controlling Disease, U. S. P. Units/Day
Rheumatoid arthritis.....	2	Gelatin	15
	7		30
	2		45
	1		60
	1	Oil	48
	2		80
Ankylosing spondylitis.....	1	Gelatin	30
	1		60
Acute scleroderma.....	1	Gelatin	30
Lupus erythematosus.....	1	Gelatin	15
	1		30
	1	Oil	80
Chronic dermatitis.....	1	Gelatin	45
	1	Oil	80

face, and marked water retention have, however, occurred even with the lowest doses employed (0.19 to 0.3 mg. per day). No qualitative differences were noted with the purer preparation in the therapeutic response or in the overdosage effects. The fall of the erythrocyte sedimentation rate and the rise in 17-ketosteroid excretion

were consistent with the therapeutic efficacy of the doses used. The daily urinary 17-ketosteroid excretion of a patient receiving 0.3 mg. per day (24 units) was 47 mg., while another patient excreted 39 mg. while receiving 0.375 mg. per day of corticotropin, and 72 mg. with 0.75 mg. per day. Two patients who had received corticotropin continuously for more than one and one-half years were among the most sensitive to the therapeutic and overdosage effects of the purified preparation. A patient who offered a particularly favorable opportunity for a comparison of the potency of different preparations had been treated for rheumatoid arthritis for six months with 100 mg. per day of cortisone, with fair control of symptoms. When the treatment was changed to aqueous purified corticotropin, the same degree of control was obtained with 0.3 mg. per day (24 units). When, after seven weeks of this treatment, a standard preparation of corticotropin was used for three weeks, only minimal therapeutic effects were obtained with 60 units per day. At this point, 30 units per day (0.375 mg.) of aqueous purified corticotropin produced prompt and complete improvement.

By comparison with less potent preparations, purified corticotropin appeared to be about twice as effective clinically as would be expected from the unit potency determined by animal assay. Similar clinical responses were obtained with daily doses of 90 units of a glacial acetic acid extract of pig pituitary powder (2 units per milligram), 60 units of a cellulose-purified preparation (20 units per milligram), and 45 units of the oxycellulose-purified material (80 units per milligram) employed in this study. This difference is not attributable to an error in the bioassay, for the purified material was also twice as active as the equivalent amount of the cruder product from which it was derived.⁵

The reason for the increased efficiency has not been established, but it may be related to increased stability of purified corticotropin in body fluids. It has been observed that, while certain other preparations deteriorate at neutral pH,⁶ and lose corticotropic activity rapidly upon admixture with blood in vitro, the oxycellulose-purified material is stable under these conditions.⁷ It is of interest that a satisfactory response has been obtained with purified corticotropin prepared from pig pituitaries in patients who had become unresponsive to standard preparations derived from the same species.⁸ The possibility that cruder preparations may contain destructive contaminants is suggested by the recent demonstration of two proteolytic enzymes in an extract of standard potency.⁹ However, the increased efficiency of purified corticotropin could also conceivably result from the removal, during purification, of physiologically antagonistic substances.

It is of interest that corticotropin, at this stage of purity, is 150 times as effective clinically as the standard corticotropin and at least 250 times as effective on a weight basis as cortisone. In the purification of corticotropin by the oxycellulose method, 90% of the hormone in a glacial acetic extract is recovered in the purified fraction. The increased therapeutic efficiency achieved by purification reduces the dosage requirement and thus in effect makes available an increased amount of corticotropin for clinical use. These findings indicate that newer

concentrates of corticotropin differing in purity or in method of preparation will require clinical evaluation to determine dosage and frequency of administration.

Harrison Ave. and Bennet St. (Dr. Astwood).

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STERILE LANCETS FOR BLOOD SAMPLING

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William P. Murphy Jr., M.D., Boston

and

Frank C. Comploier, B.S., Washington, D. C.

Among the epidemiological factors in the transmission of homologous serum jaundice, the spread via cannulated needles used for obtaining blood samples and tattooing needles has been substantiated.¹ The possibility of needle transmission of poliomyelitis has been empha-

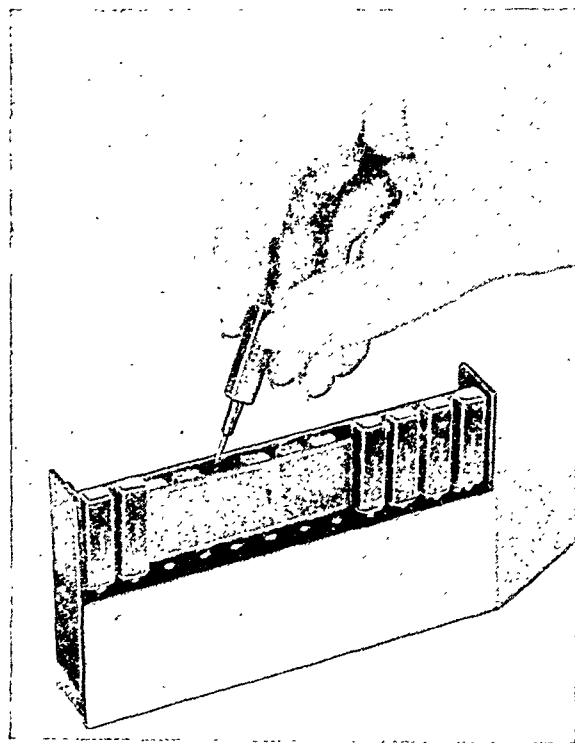


Fig. 1.—Case of stainless steel lancets for safe acupuncture.

sized.² Sterilization in saturated steam at 121 C or dry heat at 160 C is essential, because chemical disinfection is inadequate against the virus concerned.

Surgeon, Peter Bent Brigham Hospital, and Assistant Clinical Professor of Surgery, Harvard Medical School (Dr. Walter); Research Fellow in Medicine, Peter Bent Brigham Hospital (Dr. Murphy); and Technical Assistant to the Medical Director, National Blood Program, American Red Cross (Mr. Comploier).

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2. Lenard, A.: Poliomyelitis: The Possibility of Syringe Transmission, *M. Times* 79:395 (July) 1951.

Safe acupuncture of the individual patient presents problems in packaging, sterilizing, and dispensing lancets. Accidental pricking of the fingers of technicians and supply room workers must be guarded against. In hospital and clinic practice and blood donor evaluation, so many lancets are used that maintenance of sharpness, the provision for automatic cleaning, and prevention of loss are major considerations. A technique is presented that accomplishes these ends.

The lancets (fig. 1) are made of a piece of cutlery stainless steel embedded in a waterproof nylon handle. The piercing tip is ground in the shape of apposed hyperbolic sections as in the conventional harness maker's awl. The sharp hyperbolic edge cuts skin cleanly without tearing or stretching. The incision is not painful and bleeds freely. The handle has a conical section at the blade end, which serves as a plug to hold the instrument in the case.

The lancet case is designed to provide for cleaning, sterilization, storage, dispensing, and discard of the lancets. It is molded of heat-resistant plastic. The front step of the case has a series of tapered pockets, into

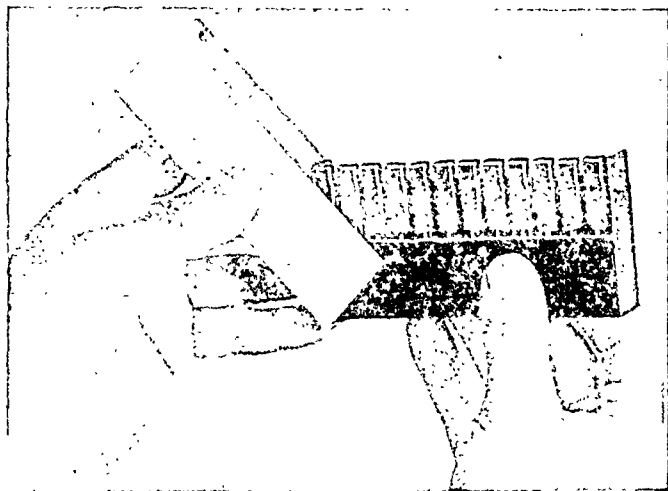


Fig. 2.—Removing cover from lancet case to expose lancets.

which the freshly rinsed lancets are plugged prior to sterilization. The aluminum cover is slid into place, and sterilization is accomplished by exposure to saturated steam at 121 C for 30 minutes. The lancets fit in the case snugly enough to keep them sterile until used.

The lancets are dispensed either by sliding the cover over the end to expose the handles or by lifting up and swinging down one end (fig. 2), so that the cover can be slid under the case as a base. As the individual lancets are used, they are discarded into the open slots in the rear step, where they become inaccessible for reuse (fig. 1) and where the protected points are exposed for inspection and cleaning.

When all the lancets are in the discard slots, they are cleaned by standing the case in 2 cm. of detergent for 10 minutes. The case is then held bottom side up under running tap water to rinse off the detergent. The cover is removed, and the lancets are spilled onto a paper towel. The lancets are plugged into the wet tapered holes, and the cover is replaced prior to sterilization.

SUMMARY

Equipment and technique are described for the accomplishment of safe acupuncture.

COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, M.D., Secretary.

Meth-Dia-Mer-Sulfonamides (See New and Nonofficial Remedies 1951, page 103).

Suspension Meth-Dia-Mer-Sulfonamides: 473 cc. bottles. A suspension containing 29 mg. each of sulfadiazine, sulfamerazine, and sulfamethazine in each cubic centimeter. Premo Pharmaceutical Laboratories, Inc., South Hackensack, N. J.

Tablets Multazine: 0.5 gm. Each tablet contains 0.167 gm. each of sulfadiazine, sulfamerazine and sulfamethazine. Kremers-Urban Company, Milwaukee, Wis.

Tablets Meth-Dia-Mer-Sulfonamides: 0.5 gm. Each tablet contains 0.167 gm. each of sulfadiazine, sulfamerazine and sulfamethazine. Premo Pharmaceutical Laboratories, Inc., South Hackensack, N. J.

Protein Hydrolysates (See New and Nonofficial Remedies 1951, page 400).

Solution Hyprotigen 6%: 500 cc. and 1,000 cc. bottles. An enzymatic hydrolysate of casein containing amino acids and polypeptides. It contains approximately 55% of its total nitrogen as alpha amino nitrogen. U. S. Trademark 434,994. Don Baxter, Inc., Glendale, Calif.

Solution Hyprotigen 6% with Dextrose 5%: 500 cc. and 1,000 cc. bottles. An enzymatic hydrolysate of casein containing amino acids and polypeptides. It contains approximately 55% of its total nitrogen as alpha amino nitrogen. U. S. Trademark 434,994. Don Baxter, Inc., Glendale, Calif.

p-Aminosalicylic Acid (See New and Nonofficial Remedies 1951, page 89).

Powder Parasal: 113.4 gm., 226.8 gm., and 453.6 gm. bottles. Bulk; 11.34 kg. and 22.68 kg. drums for compounding use. U. S. Trademark 585,718. The Panray Corporation, New York.

Tablets Parasal: 0.5 gm. U. S. Trademark 585,718. The Panray Corporation, New York.

Mannitol Hexanitrate (See New and Nonofficial Remedies 1951, page 232).

Tablets Mannitol Hexanitrate: 16 mg. and 32 mg. Direct Laboratories, Inc., Buffalo, N. Y.

Tablets Mannitol Hexanitrate: 32 mg. Raymer Pharmacal Company, Philadelphia.

Progesterone-U.S.P. (See New and Nonofficial Remedies 1951, page 361).

Solution Progesterone in Oil: 10 cc. vials. A solution in sesame oil containing 10 mg. of progesterone in each cubic centimeter. Preserved with 0.5% chlorobutanol. Kremers-Urban Company, Milwaukee, Wis.

Aminophylline-U.S.P. (See New and Nonofficial Remedies 1951, page 299).

Solution Aminophylline: 10 cc. ampuls. A solution containing 25 mg. of aminophylline in each cubic centimeter. The Blue Line Chemical Company, St. Louis.

Methimazole (See THE JOURNAL, Dec. 22, 1951, page 1668).
Tablets Tapazole: 10 mg. Eli Lilly & Company, Indianapolis, Ind.

COUNCIL ON PHYSICAL MEDICINE AND REHABILITATION

The Council on Physical Medicine and Rehabilitation has authorized publication of the following reports.

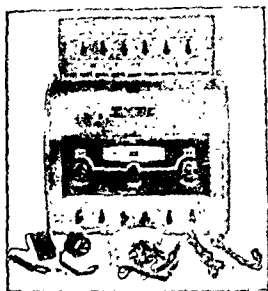
RALPH E. DE FOREST, M.D., Secretary.

MAICO AUDIOMETER, MODEL E-2, ACCEPTED

Manufacturer: The Maico Company, Inc., 21 N. Third St., Minneapolis 1.

The Maico Audiometer, Model E-2, is designed as a two-channel, pure tone instrument for research purposes. The apparatus includes a pair of matched air receivers (one for each channel) and a calibrated bone conduction unit.

The instrument operates on alternating current of 25 or 60 cycles at 110-120 volts or 220-240 volts. It draws 0.5 ampere at 115 volts and 0.25 ampere at 230 volts; so that the wattage is 60. It measures 35 (height) by 57 by 32 cm. (13½ by 22½ by 12½ in.) and weighs 19.5 kg. (43.5 lb.).



Maico Audiometer, Model E-2

The instrument consists of one main oscillator providing the standard audiometer test tones, one auxiliary oscillator providing a 1,000-cycle reference tone, and a masking oscillator. There are two output channels with separately controlled attenuators. The output from Channel 1 may be either the standard test tones for air

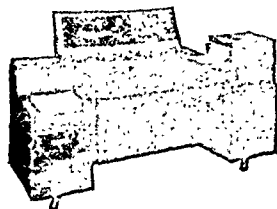
or bone conduction, or microphone speech for air or bone conduction. The output from Channel 2 may be the standard test tones, the 1,000-cycle reference tone, the masking tone, or the microphone for air conduction only. The frequencies supplied from both channels are 125, 250, 500, 1,000, 2,000, 3,000, 4,000, 6,000, 8,000, and 10,000 cps.

Evidence from a laboratory acceptable to the Council indicated that this instrument satisfied the minimum requirements of the Council for pure tone audiometers. The Council on Physical Medicine and Rehabilitation voted to include the Maico Audiometer, Model E-2, in its list of accepted devices.

OFFNER ELECTROENCEPHALOGRAPH, TYPE D, ACCEPTED

Manufacturer: Offner Electronics Inc., 5320 N. Kedzie Ave., Chicago 25.

The Offner Electroencephalograph, Type D, is a six or eight channel ink-writing instrument. In general appearance it resembles a writing desk which can be moved about on casters.



Offner Electroencephalograph,
Type D

It measures approximately 100 (height) by 180 by 90 cm. (3½ by 6 by 3 ft.) and weighs 272 kg. (600 lb.). Crated for shipment it measures 118 by 202 by 100 cm. (46½ by 79½ by 39½ in.) and weighs 364 kg. (801 lb.). It operates entirely from 50 or 60 cycle alternating current power lines, at 105 to 125 volts, and draws 500 watts. No batteries are used.

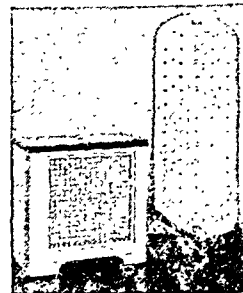
Clinical and electrophysical observations in laboratories acceptable to the Council gave evidence that the instrument was soundly constructed and performed as represented by the manufacturer.

The Council on Physical Medicine and Rehabilitation voted to include the Offner Electroencephalograph, Type D, in its list of accepted devices.

HYDRO-PNEUMATIC BATH ACCEPTED

Manufacturer: Jay H. Meseroll, 130 S. 19th St., Philadelphia 3.

The Hydro-Pneumatic Bath, formerly named the Massage Master Bath, Model M, is a device designed for use in connection with a bath tub in such a way as to agitate and aerate the water. It consists of two principal parts: (1) a perforated plate of stainless steel which lies on the bottom of the tub and bears the weight of the patient and (2) a control unit consisting of an electrically driven air pump housed in a cabinet. The steel plate or bath unit measures 117 by 44 cm. (46 by 17½ in.) and weighs 16 kg. (35 lb.). The control unit measures 62 (height) by 61 by 41 cm. (24½ by 24 by 16 in.) and weighs 63 kg. (140 lb.). The combined shipping weight of the two units when packed is 113 kg. (250 lb.).



Hydro-Pneumatic Bath

The motor in the control unit requires a 60 cycle alternating current at 115 volts and draws 500 watts of power.

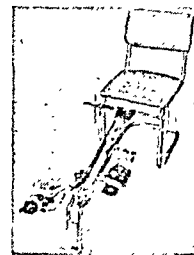
Evidence of sound construction and satisfactory performance was obtained from a source acceptable to the Council. The occasional addition of hot water while the bath is in use may be necessary in order to keep the temperature reasonably constant. Therapeutic benefits to be anticipated are those recognized for agitated warm baths in general. The Council on Physical Medicine and Rehabilitation voted to include the Hydro-Pneumatic Bath in its list of accepted devices.

RESTORATOR ACCEPTED

Manufacturer: Rudolph J. Boyko, 640 Madison Ave., New York 22.

The Restorator is a device for administering active exercise in the form of a circular alternating movement like that made in pedaling a bicycle. The exercise can be carried out by either hands or feet. The distinctive feature of this device is the absence of a seat. The patient remains in bed or on whatever chair he is occupying. The apparatus is light, portable, and versatile. The pedal arms can be provided with extensions long enough to make a sort of shoulder wheel.

The over-all measurements of the apparatus when unpacked are 23 (height) by 79 by 41 cm. (9 by 31 by 16 in.), and it weighs 7.7 kg. (17 lb.). The shipping weight is 9 kg. (20 lb.); the package measures 28 by 84 by 46 cm. (11 by 33 by 18 in.). Evidence from sources acceptable to the Council indicated that this device is useful in exercises for the foot, ankle, leg, hip, wrist, arm, and shoulder provided patients are carefully instructed in its use. The Council on Physical Medicine and Rehabilitation voted to include the Restorator in its list of accepted devices.



Restorator

HEALTH RESORT FACILITIES OF THE LEO N. LEVI MEMORIAL HEALTH RESORT ACCEPTED

Operating Agency: Leo N. Levi Memorial Hospital, Prospect Ave., Hot Springs, Ark.

The Leo N. Levi Memorial Hospital was established in 1914 and has 116 beds. The hospital is approved by the Council on Medical Education and Hospitals for the training of resident physicians and also by the American College of Surgeons. The mineral water, the same as that supplied to all of the health resorts at Hot Springs, is available both for drinking and for bathing, and no special therapeutic claims are made for it. Evidence from sources acceptable to the Council showed that the resort was well managed, had good medical supervision, and satisfied requirements of the Advisory Committee on A Health Resorts. The Council on Physical Medicine and Rehabilitation voted to include the Health Resort facilities of the Leo N. Levi Memorial Hospital in its

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AMERICAN MEDICAL EDUCATION
FOUNDATION

The year 1952 will be the greatest in history for voluntary philanthropy and for the American Medical Education Foundation, according to leading speakers at the Feb. 17 meeting of American Medical Education Foundation. Leaders from 40 states met at the Sheraton Hotel, Chicago, to start the 1952 campaign. A minimum of 2 million dollars from the medical profession is the goal in 1952, according to Dr. Elmer L. Henderson, Foundation President and Chairman of the one day workshop. He reported the receipt of 720 individual contributions totaling more than \$40,000 in the first six weeks of 1952, which he believes gives promise that the goal can be reached.

Dr. James E. Almond, Chicago, president of the American City Bureau and a pioneer among fund raising counselors, in the principal address commended the medical profession for the start that was made in 1951 toward solving the problems of medical school financing. Dr. Almond stimulated the group by stating that in 1952 there will be the greatest total contribution to voluntary philanthropy in the history of this country and that the sum of dollars will show a steady annual increment for a long time to come. "The penalties of leadership," said Dr. Almond, "cannot compare with its privileges. The men who are taking the initiative in this crusade will have their achievements recognized through the ministry of higher education for generations to come."

The past history and present policies of both the American Medical Education Foundation and the National Fund for Medical Education were presented by Dr. Donald G. Anderson, Secretary-Treasurer of the Foundation. Dr. Anderson also spoke on the campaign plan to be followed in 1952, which places emphasis at the so-called grass roots level. He pointed out that, since each state society is in the best position to judge what kind of a campaign will be most effective among its membership, the decision in this matter is being left to each society. It is hoped, however, that each society will work out a plan for approaching its members individually as well as through mass media. Each state should set its own goal as to the amount it thinks it can raise. The Founda-

tion has set a minimum goal of 2 million dollars for 1952, and hopes to secure contributions from a large number of physicians. If enough physicians contribute, the amount can be obtained from them alone. The individual physician should determine the amount of his own contribution, although it should be clear that token gifts alone will not raise the money that is needed. The 1952 drive calls for an intensive effort during the months of April, May, and June, with the remainder of the year being devoted to completion of local campaigns and to securing special gifts from various sources within the medical profession.

R. F. Staudacher, Executive Secretary of the American Medical Education Foundation, discussed the materials and campaign aids available for use throughout the country. The experiences of several states during the 1951 drive were outlined by Drs. John W. Green, California; Atha Thomas, Colorado; W. G. H. Dobbs, Connecticut; J. W. Denny, Indiana; Newland E. Day, Maryland; Thomas H. Lanman, Massachusetts; J. Stanley Kenney, New York; William J. Orr, New York, and Walter F. Donaldson, Pennsylvania.

It was evident at this meeting that there is sufficient enthusiasm among the leaders in the drive to justify hope for successful completion of the campaign to raise funds for medical education. More help is needed, particularly at the local level, and if physicians are interested in solving their own problems they should volunteer to give money and time. A commendable start has been made, but the impetus for a driving campaign must come from the profession as a whole.

MISINTERPRETATION OF "NEEDS"
FOR MEDICAL CARE

Comparisons between the practice of law and the practice of medicine can be helpful or misleading. Studies in recent years of the unmet needs for legal and medical services seem to provide some useful comparisons. The term "unmet needs" for legal and medical services has, however, been used in a fashion that implies unmet desires, whims, or mere wants; moreover, for the purposes of medical economics, the term "unmet needs" as used in these studies is quite awkward, because it does not imply that these "needs" are sufficiently acute to induce the individual to seek medical care. The medical economist would prefer the term "demand," because it implies needs or wants coupled with the ability and willingness to actually seek medical attention. If this particular use of the term "unmet needs" is kept in mind, these recent studies do provide some helpful comparisons between the practice of law and the practice of medicine.

In 1948, the American Bar Association, as a part of its Survey of the Legal Profession, published a study by Koos of family needs for legal services.¹ In 1950 Michigan State College published a study by Hoffer and others of the unmet needs for medical services in certain Michigan communities.² Koos concluded that the families covered in his survey failed by varying margins to obtain the quantity and quality of legal services that Koos considered reasonably necessary to meet the family needs for legal services. He also gave considerable attention to the

1. Koos, E. L.: The Family and the Law: Survey of the Legal Profession, Boston, American Bar Association, 1949.
2. Hoffer, C. R., and others: Health Needs and Health Care in Michigan, Special Bulletin 365, East Lansing, Mich., State College Agricultural Experiment Station, Section of Sociology and Anthropology, June, 1950.

reasons for failure of the families to engage the services of lawyers. Hoffer measured the unmet needs for medical services in certain Michigan communities by interviewing persons who described symptoms for which they had neither sought nor received medical attention. Spot checks were made by physicians to determine the reliability of the self-diagnoses as a method of measuring unmet needs. Hoffer, like Koos, was interested in the reasons given during the interview for not seeking and obtaining professional services.

Similar studies of the unmet needs for dental services, for the services of accountants, engineers, and other professional persons are not available, but such studies should make possible similar evaluation of relative unmet needs. Indeed, it would be necessary to have studies of the unmet needs for all important commodities and services before one could appraise the relative standing or rank of unmet needs for any one commodity or service. Until such additional studies are made no frame of reference can be found in which to evaluate the relative importance of unmet needs for medical services. Since persons literally need everything, one cannot say that the unmet needs for a particular service are great, because one does not know "how great is great" until he knows the unmet needs for many important goods and services.

There is widespread failure to realize the necessity for considering unmet needs on a relative rather than an absolute scale. The idea that human wants or needs are expandable without limit, both as to number and variety, is basic in the study of economics. Moreover, there are unmet needs for every good or service that has a price; these are the so-called economic goods and services. The persons who render these services have livings to earn for themselves and their families. Unlike air, these services command a price. If the price were higher, fewer persons would buy the service, and if the price were lower more persons would buy the service. This notion of unmet needs is, therefore, a fundamental characteristic of a system of free enterprise and free prices. There are unmet needs for every service or commodity that is sold, and the bare statement that there are unmet needs for legal and medical services is an "elucidation of the obvious."

A study, however carefully conducted, that limits itself to the unmet needs for one type of service is likely to be misinterpreted. Conclusions can be reached according to the degree of alarm one wishes to create of the frightful conditions traceable to the unmet needs for the one service under consideration. The whole person in his particular economic and social setting must be considered as the unit rather than each individual service or commodity; for example, if it could be shown that the relative degree of attainment of medical services for the people in a particular state was lower than the relative degree of attainment of legal services, dental services, or other services, one could conclude that medicine is lagging, and that the reasons for the lag should be found. But one need not rely solely on the relative position of the unmet needs for medical care; other sources of information are available, for example, mortality and morbidity rates, which reflect to a considerable extent the prevailing level of medical service.

ELECTROENCEPHALOGRAPHY AND HEARING IN YOUNG CHILDREN

A diagnosis of hearing loss in children under 3 years of age is often difficult to establish. Hearing tests that are useful in the case of adults are not applicable to such children, because they cannot reliably make their sound perception known. The background of hearing loss in young children is relatively unexplored, particularly in terms of etiology and central nervous disease.

According to Marcus and his associates,¹ electroencephalography provides a feasible means of measuring hearing acuity in young children at a time when conscious participation is not required. These investigators studied 71 patients in the clinic and by electroencephalograms taken with the patients asleep. It was noted that some children who evinced poor or no speech but good or moderately impaired hearing displayed an unusually high incidence of electroencephalographic evidence of brain damage. Of 53 children with pronounced hearing impairment, 19 had abnormal encephalograms. Electroencephalographic evidence of intracranial disorder was found in 9 of 18 children with slight to moderate hearing impairment, who had delayed, retarded, or unintelligible speech.

On the basis of these studies, the electroencephalograph appears to offer the clinician additional information regarding hearing function when viewed in its context of peripheral end organ, sensory nerve, brain stem, and cerebral ramifications and motor expression. Electroencephalography in sleep gives a qualitative estimate of the presence or absence of an intact end organ and an objective method of determining the presence or absence of brain damage to substantiate the possibility of a central nervous system defect in the hearing-speech-sensory-motor arc. Combining current otological procedures with electroencephalography in carefully selected cases enables clinicians to be more specific in differentiating between cochlear disease and central nervous system dysfunction or aphasia.

SYMPOSIUM ON PULMONARY AND CARDIAC DISEASES

A group of physicians will leave the United States about March 8 to visit Cuba, Panama, Venezuela, and the Dominican Republic, where they will present a symposium on pulmonary and cardiac diseases to the physicians of those countries. The program will consist of lectures, ward rounds, demonstrations, and operative chest surgery. The trip is sponsored by the World Medical Association in order to provide for the exchange of ideas and techniques on an international level. The World Medical Association hopes that funds will become available so that more trips of this kind can be made to other parts of the world and thus further international medical relations. Details concerning this trip will be found on page 850 in this issue of THE JOURNAL.

1. Marcus, R. E.; Gibbs, E. L., and Gibbs, F. A.: Electroencephalography in the Diagnosis of Hearing Loss in the Very Young Child, *Dis. Nerv. System* 10: 170 (June) 1949. Marcus, R. E.: Hearing and Speech Problems in Children: Observations and Use of Electroencephalography, *A. M. A. Arch. Otolaryng.* 53: 134 (Feb.) 1951.

ORGANIZATION SECTION

WORLD MEDICAL ASSOCIATION SPONSORS TRIP

The World Medical Association is sponsoring a trip to Cuba, the Dominican Republic, Panama, and Venezuela of a group of distinguished American physicians who will present a symposium on pulmonary and cardiac diseases to the physicians of those countries. The plan is one of those envisaged for the exchange of ideas and techniques on an international level and will do much to cement international medical relations.

The group making the trip will be headed by Dr. Edgar Mayer of New York, professor of clinical medicine at New York University Post-Graduate Hospital, Bellevue Medical Center, New York. Accompanying him will be: Dr. J. M. Chamberlain, chest surgeon, Bellevue and Roosevelt Hospitals, New York; Dr. Arthur Cracovaner, attending otolaryngologist at the Lenox Hill and Kingsbridge Veterans hospitals and bronchoscopist, Bellevue Hospital, New York; Dr. DeWitt Daughtry, consultant in thoracic surgery, Veterans Administration Hospital, Coral Gables, Fla., and Jackson Memorial Hospital, Miami, Fla.; Dr. Irving Kane, attending physician in pulmonary disease, Lincoln Hospital, in chest disease, Beth David Hospital, and in diagnostic roentgenology, Montefiore Hospital, New York; Dr. Earl Templeton, director and attending physician, Miami Heart Institute and St. Francis Hospital, Miami, Fla.; and Dr. Robert Wallis, attending physician, Roosevelt Hospital, New York. The majority of these physicians are members of the American College of Chest Physicians.

The program will consist of illustrated lectures, ward rounds, demonstrations, and operative chest surgery. The general topics to be discussed are: Rhinology in Pulmonary Diseases (Dr. Cracovaner), Diagnosis and Treatment of Pulmonary Diseases (Dr. Mayer), Chest Radiology (Dr. Kane), Pulmonary Surgery (Dr. Chamberlain), Diagnosis and Treatment of Heart Disease (Dr. Templeton), Cardiac Surgery (Dr. Daughtry), and Nutritional Aspects of Chronic Disease (Dr. Wallis).

The local arrangements are being made by the national medical associations of the countries to be visited. The group will leave this country about March 8, 1952, and will be away approximately three weeks. While arrangements have been made by The World Medical Association, which is sponsoring the trip, the expenses are being borne by the persons making the trip. The World Medical Association hopes that funds will become available so that more trips of this kind can be financed to other areas of the world.

FEDERAL MEDICAL LEGISLATION

Royalties for Medical Education

On Feb. 18, Representative Kennedy of Massachusetts introduced H. J. Res. 381. This resolution would provide that royalties received under certain mineral leases governing submerged lands of the Continental Shelf be set aside in the Treasury for use in grants-in-aid in medical education and research in the construction and operation of hospitals and other community health facilities. The resolution proposes that the Secretary of the Interior be authorized to grant mineral (tideland oil) leases covering the submerged lands of the Continental Shelf. Moneys received therefrom would be held in a special account in the Treasury during the present emergency. Congress could authorize the use of these funds only for urgent developments essential to the national security, including the training of physicians,

dentists, nurses, medical specialists, and technicians, and the construction of hospitals and community health facilities. After the emergency, a portion of such moneys would be used as determined by Congress as grants-in-aid for (1) medical research and education for the training of the above-mentioned group of medical and allied persons and (2) the construction and operation of hospitals and other community health facilities.

The resolution would create a National Advisory Council on Grants-in-Aid Health and Medical Education to be composed of 12 persons experienced in the fields of medical sciences, education, public health, hospital management, public administration, or related fields. It requires that this council be bipartisan, four members to be appointed by the President of the U. S., four by the President of the Senate, and four by the Speaker of the House. The council would be required to submit to Congress, not later than April 1, 1953, recommendations concerning the amount of money to be required annually for use as grants for medical education, research, construction and operation of hospitals and other community health facilities, with a plan for equitable allocation of funds.

Lincoln Treatment Investigation

Representative Rankin of Mississippi introduced H. R. 6539, which would provide for a study by the Administrator of Veterans' Affairs of the methods and practices employed by Dr. Robert E. Lincoln in the treatment of tuberculosis and cancer. The bill was introduced at the request of the AMVETS. The proposed study would be made under the direction of the Administrator of the Veterans Administration, and a report of the findings would be made to Congress within two years. The controversy over the Lincoln treatment of cancer and tuberculosis first received attention on Capitol Hill when Sen. Charles Tobey made a speech on the Senate floor and introduced several articles in the *Congressional Record*.

STATE MEDICAL LEGISLATION

Colorado

Bill Enacted.—S. 20, was approved February 8, 1952. It amended the narcotic drug act by, among other things, providing a person who sells or administers narcotic drugs to persons under the age of 21 years may be imprisoned up to 20 years. Otherwise the maximum imprisonment is 15 years.

Kentucky

Bills Introduced.—H. 279, proposes to repeal and reenact the law relating to the licensing of chiropodists and defines chiropody as the diagnosis and the local, medical, mechanical and surgical treatment of ailments of the human foot, and massage in connection therewith, except amputation of the foot or toes, or the use of anesthetics other than local, or the use of drugs or medicines other than local. H. 398, to amend the workmen's compensation act, proposes that whenever an employee is examined or treated for an industrial injury by a doctor or physician, the employer shall cause to be furnished to the employee and to the Board a copy of the report of the physician showing the examination or treatment administered. S. 166, relating to city-county boards of health and the administration of hospitals by such boards, provides, among other things, that no person taken to such a hospital for emergency treatment shall be denied admission on account of his financial condition nor shall the administration of emergency treatment to such person be delayed on account thereof. S. 184, proposes to direct the legislative research commission to make a thorough and complete investigation, study and survey of existing and required health facilities and services provided, or which should be provided, at public expense for the people of the Commonwealth.

Maryland

Bills Introduced.—H. 51, proposes to require the physical examination of food handlers at least 30 days prior to employment, showing freedom from any infectious, contagious disease. H. 63, proposes that licensed

physical therapists shall hold a doctorate degree in physical therapy from an incorporated school, college or university certified by the Maryland State Physical Therapy Society, Incorporated.

Massachusetts

Bill Introduced.—S. 351, proposes to prohibit the performance of any lobotomy, topectomy, or transorbital operation, or any brain operation designed to alleviate a functional disorder, unless the hospital staff has, by a two-thirds vote, approved the reasons for performing such operation.

Michigan

Bills Introduced.—H. 400, proposes the creation of a Michigan State Board of Naturopathy and defines naturopathy as that philosophy and practice of the healing art which embodies a complete physiotherapy and diagnosis, and which for therapeutic purposes employs nature's agencies, forces, processes and products, excepting major surgery and x-ray and radium for treatment purposes. Licentiatees would be entitled to practice naturopathy in the State of Michigan as taught in the accredited schools and colleges of naturopathy. H. 453, proposes that except as otherwise provided by law, no autopsy, post-mortem or dissection shall be performed upon the body of a deceased person except by a licensed physician who has been granted written consent therefor by which ever of the following assumes custody of the body for purposes of burial: father, mother, husband, guardian, next of kin, or in the absence of any of the foregoing, a friend or a person charged by law with the responsibility for burial. S. 314, proposes the enactment of a Michigan employee's disability benefit act.

Mississippi

Bills Introduced.—H. 89, proposes to require each applicant for a marriage license to present a certificate signed by a physician licensed to practice medicine in the State certifying freedom from venereal disease. H. 149, proposes to define the crime of abortion as willfully and knowingly by means of any instrument, medicine, drug, etc., causing any woman pregnant with child to abort or miscarry or attempting to cure or produce an abortion or miscarriage, unless the same was done as necessary for the preservation of the mother's life. The proposal would also provide that no act shall be considered as necessary for the preservation of the mother's life unless upon the prior advice, in writing, of two reputable licensed physicians. H. 234, proposes to make it unlawful for an employer to require an employee or applicant for employment to pay the cost of a medical examination or the cost of furnishing any records required by the employer as a condition of employment. H. 346, proposes that no person other than a regularly licensed druggist shall trade in marijuana and that no druggist shall trade in it either except to a regularly licensed physician or upon the prescription of such physician, which prescription shall not be used more than once and shall not be refilled. H. 347, to amend the law regulating the sale of barbiturates, proposes that when a violation of the act is committed against a minor the person so convicted shall be sentenced to the penitentiary for a term of not less than one or more than five years. S. 151, proposes an appropriation to the state medical education board for the purpose of carrying out the provisions relating to the furnishing of loans or scholarships to bona fide citizens of Mississippi for securing a medical education.

Missouri

Bill Introduced.—H. 510, proposes an amendment to the narcotic act relating to the penalty for those who unlawfully sell narcotic drugs to minors.

New York

Bills Introduced.—A.R. 138, proposes the creation of a committee to make a thorough and complete study of the alleged discriminatory action of medical schools and colleges in the selection of students because of their race or color. A. 2052 and S. 2325, to amend the medical practice act, propose to make it grounds for revocation of a license that a physician, osteopath or physiotherapist has employed, hired, procured, induced, or aided or abetted a person not licensed to practice the aforesaid professions in this state to so practice. A. 2133, to amend the public health law proposes to require physicians to immediately give notice to the health officer of the county, city, town, or village where the person resides of every case of infantile paralysis under his care. A. 2198 and S. 1919, propose an appropriation to defray the cost of research to devise a program to control and prevent infantile paralysis. A. 2255, S. 1937 and S. 2199, to amend the civil service law, propose to authorize the state comptroller to contract with a nonprofit membership corporation for the purpose of furnishing medical and surgical services and hospital services to persons employed by the state. A. 2267 and S. 2005, propose regulations for the operation of nurses registries. A. 2270 and S. 2203, to amend the education law, propose regulations for the licensing of operators of shoe fitting fluoroscopy apparatus. A. 2277 and S. 1992, propose the

creation of a state commission to make a study and survey of the prevalence and facilities for the treatment of all forms of heart disease. A. 2373, to amend the workmen's compensation law, proposes to prohibit physicians designated by the board to conduct special examinations from examining, treating, or prescribing for claimants. A. 2531, proposes the creation of a permanent hospital survey and planning commission for the state for the purpose of inventorying existing hospital facilities and carrying out construction programs for additional necessary hospitals. A. 2606, to amend the public health law, proposes to require the commissioner of public health to safely keep and preserve all hospital records for any public or private hospital which discontinued operations for any reason and which failed to arrange for the preservation of its records. A. 2636, to amend the public health law, proposes to require physicians to report to the state department of health promptly the name and if possible the address of any person under treatment if it appears that such person is an habitual user of any narcotic drug. S. 1753, to amend the penal law, proposes to make it unlawful for the trustees, superintendents and managers of nonsectarian hospitals to refuse to employ physicians or refuse to allow physicians or nurses to use the facilities of the hospital or to practice his profession therein because of race, color, creed, or religion. S. 1849, to amend the vehicle and traffic law, proposes to make it unlawful for any habitual user of a narcotic drug to operate a motor vehicle while under the influence of such drug. S. 1856, to amend the education law, proposes to permit an applicant for a license to practice physiotherapy to practice physiotherapy during the pendency of the granting or denial of such application. S. 1857, to amend the education law, proposes to authorize applicants for a license to practice nursing to practice their profession pending the granting or denial of such application. S. 1995, to amend the public health law, proposes to establish within the department of health an adult hygiene and geriatrics program to improve and protect the health and vitality of middle and elderly citizens in the state. S. 1997, proposes an appropriation for the purpose of conducting experiments, in cooperation with the medical society of New York State, in mass detecting of diseases in their early stages through the process of multiphasic screening. S. 2007, proposes an appropriation for the purpose of establishing an experimental geriatric clinic. S. 2118, proposes to authorize the board of medical examiners to regulate and license the practice of corrective therapy which term is defined as being synonymous to exercise therapy, corrective physical education, and physical reconditionings. S. 2178, to amend the education law, proposes to exempt from labeling provisions the sale of proprietary drugs except those which are poisonous, habit forming and/or because of their toxicity or other potentiality for harmful effect, or the method of their use, or the collateral measures necessary to their use, are not safe for use except under the supervision of a practitioner licensed by law to administer such medicines. S. 2216, proposes to require secondary schools to include instruction in the nature and effect on human system of narcotic and habit-forming drugs. S. 2416, proposes that in any case in which the state or political subdivision of the state contributes part or all of the costs for medical or dental indemnity or hospital service, the subscriber shall have the right to select for such expense indemnity or service any nonprofit medical care plan authorized and approved by the superintendent of insurance.

Rhode Island

Bill Introduced.—S. 132, proposes regulations for the licensing of professional and practical nurses.

South Carolina

Bill Introduced.—H. 1813, proposes the establishment of a state board of health.

Virginia

Bills Introduced.—H. 569, proposes regulations for the licensing of ophthalmic dispensers. H. 651, proposes regulations for the awarding of scholarships for graduate instruction in nursing.

SUPPLEMENT AVAILABLE TO REVIEWS OF MEDICAL MOTION PICTURES

The Committee on Medical Motion Pictures has completed the 1951 supplement to the second revised edition of the booklet entitled "Reviews of Medical Motion Pictures." This supplement contains 90 reviews of medical and health films reviewed in THE JOURNAL from Jan. 1, 1951, through Dec. 31, 1951. Each film has been indexed according to subject matter. The purpose of these reviews is to provide a brief description and an evaluation of motion pictures that are available to the medical profession. Copies have been sent to the secretary of each of the state medical societies. Complimentary copies will be sent to county medical societies and other medical organizations on request.

MEDICAL NEWS

ALABAMA

Pediatric Society to Honor Dr. Alfred Walker.—The 28th annual meeting of the Alabama State Pediatric Society in Montgomery April 16 will be dedicated to Dr. Alfred A. Walker, Birmingham. The speakers will be Drs. Francis F. Schwenker, Baltimore, and William A. Reilly, San Francisco. Dr. Hughes Kennedy of Birmingham will give the address of tribute to Dr. Walker. Dr. Walker is emeritus professor of pediatrics at the Medical College of Alabama. He has been chairman of the Jefferson County Board of Health since 1933 and was a director of the American Board of Pediatrics from 1934 to 1944. All pediatricians and all of Dr. Walker's friends are invited to this meeting. Correspondence should be addressed to Dr. David B. Monsky, president of the Alabama State Pediatric Society, 732 Adams Ave., Montgomery.

CALIFORNIA

Dr. Sox Succeeds Dr. Geiger.—Dr. Ellis D. Sox has been named health director of the City of San Francisco and took over his duties Feb. 26. He left his position as chief of the division of local health service for the California State Department of Public Health. Dr. Sox has been health officer of Tulare County and joined the state health department some years ago on the recommendation of Dr. Geiger to study the health of migratory workers.

Personals.—Dr. Edwin B. McLean, formerly with Smith, Kline & French Laboratories in Philadelphia, has joined Cutter Laboratories, Berkeley, as director of clinical investigation. Dr. John C. Ruddock, a past president of the Los Angeles County Medical Association, and now medical director, Richfield Oil Corporation, Los Angeles, has been elected an honorary member of the Royal Society of Medicine of London, England, "in recognition of distinguished services to science."

COLORADO

Gordon Goes to Baltimore.—Dr. Harry H. Gordon, Denver, has been appointed full time chief-of-staff in pediatrics, effective April 1 at Sinai Hospital in Baltimore, associate professor in pediatrics at the Johns Hopkins University School of Medicine, and pediatrician on the staff of Johns Hopkins Hospital. Dr. Gordon resigned as professor of pediatrics at the University of Colorado School of Medicine and as pediatrician-in-chief at the Colorado General and Denver General hospitals to accept these appointments.

Northeast Colorado Cancer Seminar.—A seminar on cancer, designed particularly for physicians of the northeast quarter of Colorado and southeast Wyoming, will be held April 6 in the Community Hospital at Fort Morgan. To sponsor the seminar the Northeastern Colorado Cancer Association has been created as an informal grouping of the Northeast Colorado Medical Society, the Morgan County Medical Society, and the Washington-Yuma Counties Medical Society. Interested physicians, regardless of residence or membership in any of these three component societies of Colorado, are invited to attend. There will be no registration fee. The following speakers, all from Denver, will appear on the program:

- Emmett A. Mechler, Cancer of the Cervix and Uterus.
- Harry W. LeFevre, Cancer of the Colon.
- Kenneth D. A. Allen and John H. Freed, Cancer of the Breast from the Radiologists' Standpoint.
- Karl F. Sunderland, Cancer of the Breast from the Surgeon's Standpoint.
- Peter C. Hoch, Cancer in Childhood.
- Henry M. Lewis, Cancer of the Skin.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

FLORIDA

Pharmacy Sells Both the Drug and the Prescription.—Conviction of a Jacksonville physician for aiding and abetting the violation of the Food, Drug and Cosmetic Act was reported by the Food and Drug Administration, Washington, D. C., Feb. 19. The physician, Dr. Roosevelt F. Mills, is said to have furnished a drug store with signed prescription blanks, which the pharmacists used for sales of sulfathiazole and penicillin to persons Dr. Mills did not know and who were not his patients. A Food and Drug Administration inspector investigating the practices of the Imperial Pharmacy in Jacksonville attempted to buy a "sulfa treatment" without a prescription and was told by one of the pharmacists that a prescription was required, but he could sell him both the drug and the prescription. The pharmacist filled in the inspector's name and other prescription data on one of the blanks signed by Dr. Mills and put a dollar for Dr. Mills in the same drawer with the signed blanks. By tracing other purchasers named on filed prescriptions signed by Dr. Mills, the inspectors found young men who testified before the jury to similar experiences when they had approached the pharmacists for venereal disease treatments. The drug store owner, L. S. Kilbee, and his pharmacists, J. S. Bernreuter and I. M. Seay, did not contest the illegal sales charges, which included sales of barbiturates without prescription. Judge Bryan Simpson fined all four persons after the jury verdict in the Mills trial was announced.

ILLINOIS

Meeting on Ophthalmology and Otolaryngology.—The annual convention of the Central Illinois Society of Ophthalmology and Otolaryngology will be held March 28-30 at the Abraham Lincoln Hotel in Springfield under the presidency of Dr. Grover C. Otrich, Belleville. Out-of-state speakers will be Dr. James B. Costen, St. Louis, who will speak on "Morphology of Tumors of the Larynx," and Dr. Trygve Gundersen, Boston, whose subject will be "Herpes Simplex Corneae." At the banquet Saturday evening, J. J. Miller, director of research and technology, J. R. Roerig and Company, Chicago, will speak on "Nutrition Relative to Ophthalmology."

Chicago

Memorial Addition to La Rabida Sanitarium.—A gift of \$250,000 has been made to La Rabida Sanitarium in Jackson Park by Albert Pick, chairman of the Pick Hotels Corporation. The money will be used to construct a building adjacent to the rheumatic fever sanitarium as a memorial to Mr. Pick's first wife, who died in 1945. It will house health, home service, recreation, occupational therapy and educational activities for children. It is hoped the structure will be completed in 16 months.

Gift for Cancer Library.—A gift of \$1,500 was made to the Chicago Medical School by the Bernice Kozin Memorial Foundation, the organization's first award since it was formed a little over a year ago to raise funds for cancer research in memory of the wife of Louis Kozin. The fund will be used to buy books on cancer research for the school, the collection to be known as the Bernice Kozin Memorial Cancer Library. Mr. Sol Miller, president of the foundation, says the plan is to make this an annual gift and to increase it during the coming years.

Psychiatric Unit for Children.—Michael Reese Hospital on Feb. 18 opened a child care unit in the Institute for Psychosomatic and Psychiatric Research and Training. Children between the ages of 6 and 12 years will be accepted for observation, diagnosis, evaluation, and therapy. They will be offered the benefit of psychiatric, pediatric, psychological, electroencephalographic, and other laboratory facilities for diagnosis. Specially trained personnel in nursing, occupational therapy, and teaching specialties are available as auxiliary therapists. Beds are avail-

able for private patients of recognized psychiatrists who will be in complete charge of their patients. These psychiatrists will have the full cooperation of the resident and full time auxiliary staff of the unit. Patients with psychosomatic disorders must be under the joint care of a pediatrician and a child psychiatrist.

KANSAS

National Heart Institute Fellowship.—The National Heart Institute has awarded a fellowship in cardiovascular disease to Dr. T. K. Lin for his further study at the University of Kansas Medical Center under Dr. E. Grey Dimond, director of the cardiovascular laboratory. This is the first such fellowship to be awarded to a doctor for postgraduate study at the Kansas University Medical Center. The fellowship carries a \$300 a month stipend.

LOUISIANA

Business Men Honor Dr. Matas.—The Young Men's Business Club of New Orleans dedicated a monument Jan. 20 at Charity Hospital, New Orleans. The ceremony was in commemoration of the victory of medical science over yellow fever and in honor of Dr. Rudolph Matas, emeritus professor of surgery at Tulane University of Louisiana School of Medicine, New Orleans.

Personals.—Drs. Edmund M. Connelly and Charles S. Holbrook, psychiatrists of New Orleans, were honored at the annual staff banquet of the DePaul Sanitarium on Jan. 28, when they were presented with a plaque for distinguished and meritorious services to the institution throughout the many years since they became members of the staff. Dr. Connelly was doubly honored by receiving also a certificate and gold key from the city for the manner in which he has conducted the affairs of the City Hospital for Mental Diseases as its director. —Dr. George L. Gardiner Sr. will be the guest of honor at the first homecoming program of Gueydan High School March 19. The doctor has been practicing in Gueydan since 1915.

MARYLAND

Mount Sinai Hospital Alumni.—All former members of the house staff of the Sinai Hospital in Baltimore are requested to send their present addresses to the Office of the Director, Sinai Hospital, Baltimore.

Civil Defense Appointment.—Brig. Gen. Robert P. Williams has been appointed state deputy director of Health Services for Civil Defense to serve with Dr. Robert H. Riley, Baltimore, director, State Department of Health, and director of Health Services for Civil Defense. General Williams retired from the United States Army on Aug. 31, 1951, after 36 years of service. He is a physician who has had disaster experience during World War II and at Texas City in 1947.

MASSACHUSETTS

Tufts Alumni Association Meeting.—The Tufts Medical Alumni Association will hold its annual dinner meeting the evening of April 2 at the Somerset Hotel, Boston. The guest speaker will be Dr. Austin Smith, Chicago, Editor of *THE JOURNAL*, who will speak on "Modern Trends in Medicine." President Leonard Carmichael of Tufts College will talk on "Does New England Need State Supported Medical Schools?" Dr. Lawrence R. Dame of Greenfield, representing the 25-Year Class, will speak on "Medical Progress." Dr. Gordon M. Morrison, chairman of the dinner committee, will preside. The 25-Year Class will hold its reunion also on April 1 and 2. Preceding the dinner there will be open house at the medical school from 1 to 4 p. m.

MICHIGAN

Discussion on Industrial Health.—The University of Michigan School of Public Health, Ann Arbor, in collaboration with the Institute of Industrial Health and the school of medicine is offering a discussion on industrial health programs March 26 at the university. Out-of-state speakers include Dr. C. Richard Walmer, director of the Industrial Hygiene Foundation, Pittsburgh; Dr. Dudley A. Irwin of the Aluminum Company of America, Pittsburgh; and Dr. Seward Miller, director of the industrial hygiene division of the U. S. Public Health Service.

MINNESOTA

Annual Fahr and Duluth Clinic Lectures.—Dr. Robert E. Gross, William E. Ladd Professor of Child Surgery, Harvard Medical School, Boston, will deliver the annual George E. Fahr Lecture at the University of Minnesota on April 8 at 8 p. m. on "Coarctation of the Aorta." Dr. Gross will also take part in a continuation course in surgery to be held at the Center for Continuation Study April 7-9.

Samuel R. M. Reynolds, Ph.D., physiologist, department of embryology, Carnegie Institution of Washington, will deliver the annual Duluth Clinic Lecture at the university April 18 on "Newer Concepts of Fetal Circulation." Dr. Reynolds will also take part in a continuation course on obstetrics for specialists in that field, to be held April 17-19.

NEW YORK

State Seeks School Physicians.—The state education department has two openings in Albany at a starting salary of \$6,449 for doctors with experience as school physicians. The state civil service department is accepting applications from any qualified citizen of the United States. Applicants must have or be eligible for a New York State license to practice medicine, and have had two years of experience in the practice of medicine, including service as a school physician. The positions require much traveling. No written or oral examinations will be given. Candidates will be rated on their education and professional experience. Information may be secured from the State Department of Civil Service, State Office Building, Albany. Applications will be accepted for an indefinite period.

New York City

Society News.—Officers for the Brooklyn Urological Society for the year 1952 are Dr. Andrew J. McGowan, Ozone Park, president; Dr. Perry Katzen, Brooklyn, vice-president, and Dr. Miles W. Thomley, Brooklyn, secretary-treasurer. —At the March 27 meeting of the Kings County Radiological Society Dr. Jacob Buckstein will speak on "Tumors of the Duodenum, Jejunum and Ileum."

Annual Herter Lecture.—Dr. Arnold D. Welch, professor and director of the department of pharmacology, Western Reserve University School of Medicine, Cleveland, delivered the 48th annual Christian A. Herter Lecture Feb. 19 at the New York University College of Medicine on "Biochemical Advances in Our Knowledge of Pernicious Anemia."

Janeway Lecture at Mount Sinai Hospital.—Dr. Sidney Farber, professor of pathology at Harvard Medical School, Boston, and scientific director of the Children's Cancer Research Foundation, will deliver the Edward G. Janeway Lecture at Mount Sinai Hospital, New York, March 31 at 8:30 p. m. in Blumenthal Auditorium on "Current Research in the Chemotherapy of Cancer."

Symposium on Corticotropin and Cortisone.—This symposium is to be held by the section on microbiology of the New York Academy of Medicine on March 27-28 at the New York Academy of Medicine. Contributors to the symposium are as follows:

- Metabolism, Frank L. Engel, Durham, N. C.
- Enzymatic Reactions in Rat Tissues, Wayne W. Umbreit, Ph.D., Rahway, N. J.
- Lymphoid Tissue, William E. Ehrlich, Philadelphia.
- Loose Connective Tissue, Charles A. Ragan Jr., New York.
- Antigen-Antibody Reactions, Edward E. Fischel, New York.
- Resistance to Infections and Tumor Grafting, Herbert C. Stoerk, Rahway, N. J.
- Bronchial Asthma and Drug Idiosyncrasy, A. McGehee Harvey, Baltimore.
- Toxins and Experimental Streptococcus Hemolyticus, Lewis Thomas, Minneapolis.
- Spontaneous Trypanosomiasis, Abner Wolf, New York.
- Experimental Poliomyelitis, Gregory Schwartzman, New York.
- Bacterial Infections and Malaria, Maxwell Finland, Boston.
- Tuberculosis, Max B. Lurie, Philadelphia.
- Infections of the Eye, Alan C. Woods, Baltimore.
- Experimental Syphilis, Thomas B. Turner, Baltimore.

The meetings are open to all who are interested.

PENNSYLVANIA

Graduate Education Institute.—The spring session of the fifth annual Graduate Education Institute under the auspices of the Medical Society of the State of Pennsylvania will open in nine teaching centers throughout the state early in March with a variety of subjects covered by a teaching staff from the medical schools of Philadelphia and Pittsburgh. One day a week for five weeks lectures will be presented from 9 a. m. to 12 noon and from 1 p. m. to 4 p. m. on certain days in different centers. The centers include Allentown, Butler, Clearfield, Harrisburg, Johnstown, Lancaster, Scranton, Washington, and Williamsport. This graduate education is aimed to save the general practitioner time and expense by bringing the instruction near his home. More than 400 Pennsylvania physicians have already received certificates for having attended 70% of the lectures over a period of three years. All those taking these courses may use the credit in meeting the postgraduate education requirement of the American Academy of General Practice.

Philadelphia

Course in Diseases of the Chest.—This course, sponsored by the American College of Chest Physicians and the Laennec Society of Philadelphia, will be given March 24-28 at the Warwick Hotel in Philadelphia. In addition to speakers from Philadelphia, the following out-of-state speakers will present papers:

- Mr. William Steenken Jr., Saranac Lake, N. Y., Streptomycin in Experimental Tuberculosis.
- Nicholas D'Esopo, Sunmount, N. Y., Changing Streptomycin Regimens.
- Capt. Robert Bruce Brown, MC, USN, Bethesda, Md., Post-Traumatic Thorax.
- Coleman B. Rabin, New York, Pathology of Bronchopulmonary Tumors with Particular Reference to Adenoma.

Student General Practice Society.—Undergraduates of the University of Pennsylvania School of Medicine have set up a new medical organization, known as The General Practice Society, which reasserts the traditional ideals of the "family doctor" and emphasizes the basic role of the general practitioner as the keystone of the medical profession. More than 75 medical undergraduates at Pennsylvania have signed up for active membership. The society, according to its founders, will function primarily in the stimulation of interest in general practice, will seek to locate members in internships, residencies, and opportunities for general practice, and will promote a mutually beneficial liaison between itself and the organized specialty societies. Meetings will be held once a month to hear speakers, see appropriate motion pictures, and listen to panel discussions. Membership is open to all medical undergraduates at Pennsylvania.

TEXAS

Society News.—At the meeting of the Central Texas Journal Club at Waco on Feb. 6, Dr. S. Edward Sulkin, professor of bacteriology, spoke on "The Cocksackie Viruses—Their Role in Human Infection."

Personal.—Charles M. Pomerat, Ph.D., professor of cytology and director of the tissue culture laboratory, University of Texas Medical Branch, Galveston, will visit European cytological research centers during March, April, and May for the purpose of reporting advances in tissue culture study and of correlating European contributions in the field. Dr. Pomerat will visit medical laboratories in Paris, Milan, Zurich, Basel, Strasbourg, and Cambridge, England.

Guest Lecturers at the Medical Branch.—The following speakers will be guest lecturers at the University of Texas Medical Branch, Galveston. On March 26-28 Paul Weiss, Ph.D., professor of zoology and director of the division of biology of the University of Chicago, will describe studies on mechanisms of nerve growth and of protoplasmic synthesis. He will also discuss patterns of coordination. Dr. Stuart Mudd, professor of microbiology of the University of Pennsylvania, Philadelphia, will address staff and students and invited guests March 31 on "Microorganisms as Parasites and as Hosts."

M. F. Ashley Montagu, Ph.D., of the anthropology department of Rutgers University, New Brunswick, N. J., will speak on "Maternal Deprivation and Problems of Personality" on April 1.

VIRGINIA

Stoneburner Lectures and Symposium on Diabetes Mellitus.—Dr. Garfield G. Duncan, clinical professor of medicine, Jefferson Medical College of Philadelphia, will deliver the fifth annual Stoneburner lecture series at the Medical College of Virginia, Richmond. The first lecture will be at 8:30 p. m. March 19 on "Management of Diabetes Mellitus," and the second lecture at the same time March 20 will be on "Consideration of the Undernourished Patient."

A symposium on diabetes mellitus and nutrition will be held in the auditorium March 20-21. Out-of-state speakers and the subjects of one of their papers are as follows:

- Alfred E. Wilhelmi, Ph.D., Atlanta, Carbohydrate Metabolism.
- Henry T. Ricketts, Chicago, Serum Lipids and Atherosclerosis.
- Priscilla White, Boston, Diabetes in Childhood.
- John B. McKittrick, Boston, Evaluation of Lower Extremity Lesions in the Patient with Diabetes Mellitus.
- J. Russell Elkinton, Philadelphia, Fluid Therapy in Diabetic Acidosis.
- Stefan S. Fajans, Ann Arbor, Mich., Hypoglycemia.
- John B. Youmans, Nashville, Tenn., Vitamins and Special Diets.

The lectures were established in 1946 in memory of Captain Lewis T. Stoneburner III, MC, AUS, by his comrades at the 45th General Hospital. There is no charge for the lectures themselves. There will be a charge of \$5 a day for the symposium lectures March 20 and 21, except to members of the faculty of the Medical College of Virginia, the Medical Department of the University of Virginia, the physicians of the McGuire Veterans Hospital, medical students, and members of the house staff of any hospital.

WEST VIRGINIA

State Tuberculosis Rate Below National Average.—For the first time in history the West Virginia death rate from tuberculosis was below the national average in 1950, the state rate being 21.3% as against 22.6% for the nation. Records in the State Department of Health show that in 1951 only one-half as many people (350) died from tuberculosis as in 1947. This information is compiled from tentative figures received by the department.

State Health Department in New Offices.—Most divisions and bureaus of the state department of health were moved from the Capitol Building to the new state office building on East Washington Street in Charleston Feb. 1. The only units of the department that have not been moved are the state hygienic laboratory on McClung Street, the industrial hygiene laboratory on East Washington Street, the West Virginia Training Center for public health nurses and sanitarians, and the health information center, which are both located at the West Virginia Medical Center in South Charleston. According to Dr. Newman H. Dyer, state director of health, it is not practicable at this time to house these services in an office building owing to the nature of the work involved. He stated that, for the first time in 10 years, most of the divisions and bureaus of the department are now in one building.

WISCONSIN

Dr. W. B. Youmans to Head Department.—Dr. William B. Youmans, Portland, Ore., has been named chairman of the department of physiology at the University of Wisconsin Medical School, Madison. Dr. Youmans comes to the university from a similar post at the University of Oregon. The university is to lose the services of Dr. John A. E. Eyster, present department chairman, and Walter J. Meek, D.Sc., through retirement. Dr. Youmans had been instructor at the University of Oregon Medical School in 1938 and became head of the department of physiology in 1945. The regents approved appointment of 11 members of the Madison Veterans Administration Hospital as assistant clinical professors. Appointed were Dr. Robin N. Allin, Dr. Mark A. Foster, Dr. Anthony J. Richtsmeier, Dr. Arvin B. Weinstein, and Dr. James M. Wilkie, department of medicine; Dr. Benjamin I. Brindley, otolaryngology; Dr. Frederick G. Joachim, surgery; Dr. Palmer R. Kundert, urology; Dr. Sion C. Rogers, orthopedic surgery; Dr. Henry M. Suckle, neurosurgery; and Dr. William C. Lewis, neuropsychiatry.

GENERAL

Change Name of Society.—The name of the Association for the Study of Internal Secretions has been officially changed to The Endocrine Society. The change was made at the annual meeting in Atlantic City June 9, 1951, and became effective Jan. 1. The name of the *Journal of Clinical Endocrinology* has been changed to the *Journal of Clinical Endocrinology and Metabolism*.

Industrial Worker's Life Span Increased 20%.—Longevity among American wage earners and their families increased to a new high in 1951, with expectation of life at birth rising to 68.5 years, according to Louis I. Dublin, Ph.D., chief statistician of the Metropolitan Life Insurance Company. This is a gain of about one-fifth of a year over the 1950 figure. Since the latter part of the 19th century, expectation of life at birth has doubled in the industrial population. Among Metropolitan's industrial policyholders, average length of life has increased by five years in the past decade, and by 10 years since the early 1930's. The gains are attributed by Dr. Dublin to more healthful living and working conditions, better food, and to the outstanding gains in medical science and public health administration.

Easter Seal Campaign for the Crippled.—On March 13 the 19th annual Easter Seal Campaign will be launched by the National Society for Crippled Children and Adults and its affiliates in the 48 states, the District of Columbia, Alaska, Hawaii, and Puerto Rico. The campaign closes Easter Sunday, April 13. Direct services to more than 300,000 crippled children and adults are being given this year as the result of Easter seal contributions in the form of treatment and training, convalescent care, special education, recreation, employment opportunities, and counseling. Over 90% of the funds raised in the annual Easter seal appeal remain in the communities where they are collected, only 8.3% going to the national society for its national program of education, research, and service.

Orthopedic Surgeons Exhibit Awards.—The gold medal awards of the American Academy of Orthopaedic Surgeons for the best exhibits at the meeting in Chicago, Jan. 26-31, have been given as follows: Dr. Alfred R. Shands Jr., Col. Knox Dunlap, MC, USA, and Maj. Lucius C. Hollister, MC, USAF, Wilmington, Del., received the award for research for scientific value on an exhibit entitled "Technique for Determination of Torsion of Femur." For the best exhibit on clinical application the gold medal was given to Drs. Abel Kenin and Melvin H. Jahss, New York, for their exhibit entitled "Clinical and Pathological Follow-Up of 208 Cases of Epiphyseolysis—1 to 28 Year Follow-Up." Dr. Frederick Lee Liebolt, New York, received the gold medal for originality in presentation of his exhibit "Injuries to the Menisci of the Knee Joint."

World Health Seals.—Ten countries have declared their intention to participate in sales campaigns for "World Health Seals," which will be sold this year for the first time to promote national health programs. This announcement was made Jan. 22 by the executive board of the World Health Organization in reviewing action taken on the World Health Assembly decision of last year. The seals, depicting the Palais des Nations, WHO Headquarters, and the WHO emblem, will be put on sale on World Health Day, April 7. The proceeds will be divided between WHO and the government of the state in which seals are sold, the government retaining 75% for its health programs and WHO receiving 25%, which will be paid into a special fund to finance further issues of seals. The board learned that 26 countries will not participate this year, while 43 others had not yet made a decision.

Tuberculosis Research Grants and Fellowships.—Twenty-five grants to aid medical research projects in tuberculosis and 11 research and teaching fellowships have been approved by the board of directors of the National Tuberculosis Association for the fiscal year beginning April 1. Both the grants and fellowships were recommended by the Committee on Medical Research of the association's medical section, the American Trudeau Society. Dr. David T. Smith of Durham, N. C., is chairman of the committee. The number of investigations and the six classifications into which they fall are as follows: bacteriology and chemistry of the tubercle bacillus, six; anatomy and physi-

ology of the lung, five; pathology and immunology of tuberculosis, eight; experimental chemotherapy, one; clinical treatment of tuberculosis, three, and epidemiology of tuberculosis and related diseases, two.

College of Allergists Annual Meeting.—The annual congress of the American College of Allergists, will be at the Hotel William Penn, Pittsburgh, April 7-9, under the presidency of Dr. Harold A. Abramson, New York. The meeting will be preceded by a graduate instructional course in allergy April 4-6. The following physicians will present papers by invitation:

Horace S. Baldwin, New York, Place of the Allergist in Medical Education and Public Welfare.

Samuel M. Feinberg, Chicago, Allergy to Drugs.

Miss Cyril Bruskin, M.A., Survey of Incidence of Fungus Spores in the New Brunswick Area.

Leo H. Crippe, Pittsburgh, Regional Factors in Allergic Disease.

The guest speaker on Tuesday morning's program will be Dr. Alexander S. Wiener, New York, on "The Solution of Certain Fundamental Immunologic Problems by Studies of Rh Sensitization." Section meetings will be held Tuesday afternoon on psychosomatic, pediatric, dermatological, otolaryngological, and industrial allergy. There will be an informal banquet and dancing at 7 p. m. Tuesday.

Medical Research Awards.—At the annual meeting of the National Society for Medical Research in Chicago, Feb. 10, the board of directors voted awards to three persons and two newspapers for outstanding service to medical science. Decorative plaques will be given to Dr. William H. Bachrach of the University of Southern California, Los Angeles, for his assistance to the Southern California Society for Medical Research in its campaign to have unclaimed dogs saved for teaching and research activities. Another plaque will go to Mr. Leo Brown, now director of the department of public relations of the American Medical Association, Chicago, for his educational and organizational activities as executive secretary of the Medical Society of the State of Pennsylvania. He was especially commended for the study outline, "How Will Biological-Medical Research Help Me To Live Longer," which is now a part of the curriculum of Pennsylvania secondary schools. Dr. John R. Paine, head of the department of surgery at Buffalo General Hospital, will be honored for leadership in the program that resulted in Buffalo's city council providing for use of unclaimed animals for medical research. The two papers cited by the board were the *Chicago Tribune* and *Chicago Sun-Times* for their coverage and support in matters of the use of animals in medical studies and the procurement of dogs for those studies. Officers elected are Anton J. Carlson, Ph.D., Chicago, president, and Dr. Andrew C. Ivy, Chicago, secretary-treasurer.

FOREIGN

CARE to Establish Iron Lung Banks in Asia.—American public support of urgent health needs in various areas abroad has been undertaken by the Cooperative for American Remittances to Europe, Inc. The first part of the program, organized at the request of the World Health Organization, will be to establish three iron lung banks in Asia at a cost of \$60,000. Thirty iron lungs to be purchased will be given to three hospital centers in Tokyo, Bangkok, and a Middle Eastern city, probably Cairo. The representatives and trained personnel will be sent from the nearest center into any country stricken by an epidemic of poliomyelitis. Japan, which now averages 30,000 cases a year with a mortality rate of 25%, has no hospital equipped with an iron lung. Contributions will be accepted at CARE headquarters, 20 Broad St., New York, or at its local offices.

Health and Tuberculosis Conference in London.—A conference arranged by the National Association for the Prevention of Tuberculosis will be held in London July 8-13. It is open to all interested in preventive medicine, including the medical and veterinary professions, commercial and industrial executives, nurses, social workers, health administrators, members of public authorities, and regional hospital boards. At the last conference in 1949 over a thousand delegates from 50 countries were present.

Subjects for discussion include protective vaccination, temporary ideas in the management of tuberculous pa-

the social worker and the tuberculous family, the patient in industry, and tuberculosis in British Colonial territories. Among the speakers, according to the preliminary program, will be Dr. George C. Brink, department of health, Ontario, Canada; Dr. W. D. W. Brooks, St. Mary's Hospital, London; J. H. Carver, F.R.C.S., Hammersmith Hospital, London; A. L. D'Abreu, O.B.E., F.R.C.S., thoracic surgeon, Birmingham United Hospitals; Dr. B. A. Dormer, chief tuberculosis officer, Union of South Africa; Dr. C. M. Fletcher, pneumoconiosis research unit, M.R.C.; Prof. F. R. G. Heaf, Welsh National School of Medicine; Dr. L. E. Houghton, Harefield Hospital, Middlesex; Dr. J. B. McDougall, C.B.E., World Health Organization; Prof. R. Neubauer, Yugoslavia; Dr. F. Ridehalgh, F.R.C.P., Churchill Hospital, Oxford; T. Holmes Sellors, D.M., F.R.C.S., thoracic surgeon, Middlesex Hospital, London, and Dr. J. Greenwood Wilson, medical officer of health, City of Cardiff. A new feature of the conference will be special smaller gatherings for those with a particular interest, whether doctors, nurses, public health officials, or social workers, at which appropriate subjects will be discussed. Information can be obtained from the NAPT, Tavistock House North, Tavistock Square, London, W.C.1.

MEETINGS

AERO MEDICAL ASSOCIATION, Hotel Statler, Washington, D. C., March 17-19. Dr. Thomas H. Sutherland, 214 South State St., Marion, Ohio, Secretary.

ALABAMA, MEDICAL ASSOCIATION OF THE STATE OF, Montgomery, April 17-19. Dr. Douglas L. Cannon, 519 Dexter Ave., Montgomery, Secretary.

AMERICAN ACADEMY OF FORENSIC SCIENCES, Biltmore Hotel, Atlanta, Ga., March 6-8. Prof. Ralph F. Turner, Michigan State College Dept. of Police Administration, East Lansing, Mich., Secretary.

AMERICAN ACADEMY OF GENERAL PRACTICE, Atlantic City, N. J., March 24-27. Mr. Mac F. Cahal, 406 West 34th St., Kansas City 2, Mo., Executive Secretary.

AMERICAN ACADEMY OF OBSTETRICS AND GYNECOLOGY, Cincinnati, April 1. Dr. Ralph A. Reis, 116 South Michigan Boulevard, Chicago 3, Secretary.

AMERICAN ACADEMY OF NEUROLOGY, Brown Hotel, Louisville, Ky., Apr. 24-25. Dr. Francis M. Forster, 3800 Reservoir Rd. N.W., Washington, D. C., Secretary.

AMERICAN ASSOCIATION OF ANATOMISTS, Providence, R. I., March 19-21. Dr. Normand L. Hoerr, 2109 Adelbert Road, Cleveland 6, Secretary.

AMERICAN ASSOCIATION OF IMMUNOLOGISTS, New York, April 14. Dr. John Y. Sugg, 1300 York Ave., New York, Secretary.

AMERICAN ASSOCIATION OF INDUSTRIAL PHYSICIANS AND SURGEONS, Cincinnati, April 21-24. Dr. Edward C. Holmblad, 28 E. Jackson Blvd., Chicago 4, Managing Director.

AMERICAN ASSOCIATION OF PATHOLOGISTS AND BACTERIOLOGISTS, New York, April 10-12. Dr. Alan R. Moritz, 2085 Adelbert Road, Cleveland 6, Secretary.

AMERICAN ASSOCIATION OF RAILWAY SURGEONS, Drake Hotel, Chicago, April 1-3. Dr. Chester C. Guy, 5800 Stony Island Ave., Chicago 37, Secretary.

AMERICAN COLLEGE OF ALLERGISTS, William Penn Hotel, Pittsburgh, April 7-9. Dr. Fred W. Wittich, 423 LaSalle Medical Bldg., Minneapolis 2, Secretary.

AMERICAN COLLEGE OF PHYSICIANS, Cleveland, April 21-25. Mr. E. R. Loveland, 4200 Pine St., Philadelphia 4, Executive Secretary.

AMERICAN COLLEGE OF SURGEONS, SECTIONAL MEETINGS:
Minneapolis, Radisson Hotel, March 24-26. Dr. Harvey Nelson, 78 South 9th St., Minneapolis 2, Chairman.
Tucson, Ariz., Pioneer Hotel, April 7-9. Dr. Meade Clyne, 110 South Scott St., Tucson, Chairman.
Vancouver, B. C., Vancouver Hotel, March 31-April 4. Dr. J. Russell Neilson, 925 West Georgia St., Vancouver, B. C., Chairman.

AMERICAN CONGRESS ON OBSTETRICS AND GYNECOLOGY, Netherlands-Plaza Hotel, Cincinnati, March 31-April 4. Dr. Luella E. Nadelhoffer, 116 South Michigan Ave., Chicago 3, Secretary.

AMERICAN DERMATOLOGICAL ASSOCIATION, Broadmoor Hotel, Colorado Springs, Colo., Apr. 23-26. Dr. Louis A. Brunsting, 102 Second Ave. S.W., Rochester, Minn., Secretary.

AMERICAN HEART ASSOCIATION, Hotel Statler, Cleveland, April 17-20. Dr. William H. Bunn, 1775 Broadway, New York 19, Secretary.

AMERICAN PSYCHOSOMATIC SOCIETY, Chicago, March 29-30. Dr. Frederick C. Redlich, 551 Madison Avenue, New York 22, Secretary.

AMERICAN SOCIETY FOR EXPERIMENTAL PATHOLOGY, New Orleans 12, Secretary. Dr. Russell L. Holman, 1542 Tulane Ave., New Orleans 12, Secretary.

AMERICAN SOCIETY FOR PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, Hotel Statler, New York, April 14-18. Dr. Carl C. Pfeiffer, 1835 W. Polk St., Chicago 12, Secretary.

AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, New York, April 14-18. Dr. Elmer H. Stotz, 260 Crittenden Blvd., Rochester, N. Y., Secretary.

AMERICAN SURGICAL ASSOCIATION, White Sulphur Springs, W. Va., Apr. 16-18. Dr. Nathan A. Womack, University Hospitals, Iowa City, Secretary.

ARIZONA MEDICAL ASSOCIATION, Phoenix, April 30-May 3. Dr. Frank J. Milloy, 15 E. Monroe St., Phoenix, Secretary.

ARKANSAS MEDICAL SOCIETY, Little Rock, April 21-23. Dr. William R. Brooksher, 215 Kelley Bldg., Fort Smith, Secretary.

CALIFORNIA MEDICAL ASSOCIATION, Biltmore Hotel, Los Angeles, April 27-30. Dr. Albert C. Daniels, 450 Sutter St., San Francisco 8, Secretary.

CONNECTICUT STATE MEDICAL SOCIETY, Hartford, April 29-May 1. Dr. Creighton Barker, 160 St. Ronan Street, New Haven, Secretary.

FLORIDA MEDICAL ASSOCIATION, Hollywood, April 27-30. Dr. Samuel M. Day, P. O. Box 1018, Jacksonville, Secretary.

IOWA STATE MEDICAL SOCIETY, Des Moines, April 28-30. Dr. Allan B. Phillips, 406 Sixth Avenue, Des Moines 9, Secretary.

JOHN A. ANDREW CLINICAL SOCIETY, Memorial Hospital, Tuskegee Institute, Ala., April 6-12. Dr. Eugene H. Dibble Jr., Memorial Hospital, Tuskegee Institute, Secretary.

KANSAS MEDICAL SOCIETY, Town House, Kansas City, April 27-May 1. Dr. Dale D. Vermillion, 512 New England Bldg., Topeka, Secretary.

LOUISIANA STATE MEDICAL SOCIETY, Shreveport, April 28-30. Dr. C. Grenes Cole, 1430 Tulane Ave., New Orleans 12, Secretary.

MARYLAND, MEDICAL AND CHIRURGICAL FACULTY OF THE STATE OF, Baltimore, April 28-30. Dr. George H. Yeager, 1211 Cathedral St., Baltimore 1, Secretary.

MICHIGAN CLINICAL INSTITUTE, Book-Cadillac Hotel, Detroit, March 12-14. Dr. E. F. Sladek, 606 Townsend St., Lansing 15, Chairman.

MID-CONTINENT PSYCHIATRIC ASSOCIATION, President Hotel, Kansas City, Mo., April 26-27. Dr. Paul Hines, 2625 W. Paseo, Kansas City, Mo., Secretary.

MISSOURI STATE MEDICAL ASSOCIATION, Hotel Jefferson, St. Louis, March 30-April 2. Dr. H. E. Petersen, 634 North Grand Blvd., St. Louis 3, Secretary.

NEW ORLEANS GRADUATE MEDICAL ASSEMBLY, Municipal Auditorium, New Orleans, March 10-13. Dr. Woodward D. Beacham, 1430 Tulane Ave., Room 105, New Orleans 12, Secretary.

NORTH PACIFIC SOCIETY OF INTERNAL MEDICINE, Portland, Ore., March 22. Dr. R. L. King, 1115 Terry Ave., Seattle 1, Secretary.

PIEDMONT PROCTOLOGIC SOCIETY, Charlotte, N. C., March 29-30. Dr. B. Richard Jackson, 224 Hillsboro St., Raleigh, N. C., Secretary.

POST GRADUATE INSTITUTE OF THE PHILADELPHIA COUNTY MEDICAL SOCIETY, Bellevue-Stratford Hotel, Philadelphia, April 1-4. Dr. Thomas M. Durant, 301 South 21st St., Philadelphia 3, Director.

SOUTHEASTERN ALLERGY ASSOCIATION, Bon Air Hotel, Augusta, Ga., March 21-22. Dr. Katharine B. MacInnis, 1515 Bull St., Columbia 49, S. C., Secretary.

SOUTHEASTERN SECTION, AMERICAN UROLOGICAL ASSOCIATION, Boca Raton, Fla., April 2-5. Dr. Russell B. Carson, Sweet Bldg., Fort Lauderdale, Fla., Secretary.

SOUTHEASTERN SURGICAL CONGRESS, Atlanta, Ga., March 10-13. Dr. Benjamin J. Beasley, 701 Hurt Bldg., Atlanta 3, Ga., Secretary.

TENNESSEE STATE MEDICAL ASSOCIATION, Andrew Johnson Hotel, Knoxville, April 7-9. Mr. V. O. Foster, 504 Doctors Bldg., Nashville 3, Executive Secretary.

UNITED STATES-MEXICO BORDER PUBLIC HEALTH ASSOCIATION, Monterrey, Nuevo Leon, Mexico, March 17-19. Dr. J. C. Ellington, 314 U. S. Court House, El Paso, Texas, Secretary.

INTERNATIONAL

AUSTRALASIAN MEDICAL CONGRESS, Melbourne Victoria, Australia, Aug. 22-30. Dr. C. H. Dickson, Medical Society Hall, 426 Albert St., East Melbourne, Victoria, Australia, Hon. General Secretary.

COMMONWEALTH AND EMPIRE HEALTH AND TUBERCULOSIS CONFERENCE, Central Hall, London, England, July 8-13. Dr. J. H. Harley Williams, Tavistock House North, Tavistock Sq., London, W.C.1, England, Secretary General.

CONGRESS OF THE INTERNATIONAL DIABETES FEDERATION, Leyden, Netherlands, July 7-12. Dr. F. Gerritzen, 33. Prinsegracht, The Hague, Netherlands, Secretary.

EUROPEAN CONGRESS OF CARDIOLOGY, University of London, Bloomsbury, W.C.1, England, Sept. 10-12. Dr. K. Shirley Smith, 35 Wimpole St., London, W.1, England, Secretary.

EUROPEAN SOCIETY OF CARDIOVASCULAR SURGERY, Strasbourg, France, Oct. 3-4. Sir James Learmonth, Department of Surgery, University New Buildings, Edinburgh 8, Scotland.

INTERAMERICAN CARDIOLOGICAL CONGRESS, Buenos Aires, Argentina, Aug. 31-Sept. 7. Dr. Blas Moia, Larrea 1132, Buenos Aires, Argentina, Secretary-General.

INTER-AMERICAN CONGRESS OF PUBLIC HEALTH, Havana, Cuba, Sept. 27-Oct. 1. Pan-American Sanitary Bureau, 2001 Connecticut Ave., Washington, D. C.

INTER-AMERICAN CONGRESS OF RADIOLOGY, Mexico City, Mexico, Nov. 2-6. Dr. Guido Torres Martinez, Marsella No. 11, Mexico, D.F., Secretary-General.

INTERNATIONAL COLLEGE OF SURGEONS, Madrid, Spain, May 20-24. Dr. Max Thorek, 850 West Irving Park Road, Chicago, Ill., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF COMPARATIVE PATHOLOGY, Madrid, Spain, May 4-11. Prof. Carda-Aparici, Calle Fernando VI.8, Madrid, Spain, Secretary.

INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY, London, England, July 21-26. Dr. Gordon B. Mitchell-Heggs, 5, Lisle St., London, W.C.2, England, General Secretary.

INTERNATIONAL CONGRESS ON DIABETES, Leyden, The Netherlands, July 7-12. Dr. F. Gerritzen, 33, Prinsengracht, The Hague, Netherlands.

INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST, Rio de Janeiro, Brazil, Aug. 24-30. Mr. Murray Kornfeld, 112 East Chestnut St., Chicago 11, Illinois, Executive Secretary.

INTERNATIONAL CONGRESS OF HAEMATOLOGY, Mar del Plata, Argentina, Sept. 21-26. Dr. Carlos Reussi, Anchorena 1710, Buenos Aires, Argentina, Secretary.

INTERNATIONAL CONGRESS OF HEALTH TECHNICIANS, Palais de la Mutualite, Paris, France, June 9-14. Secretariat General, 6 Square Desaix, Paris XV^e, France.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Friends House, London, N.W.1, Eng. Sept. 15-18. Sir Harold Boldero, 12 Pall Mall East, London, S.W.1, England, Secretary.

INTERNATIONAL CONGRESS ON MEDICAL RECORDS, London, England, Sept. 7-12. Miss Gwen Perkins, 120 C Street S.E., Washington, D. C., Chairman.

INTERNATIONAL CONGRESS ON NEUROPATHOLOGY, Rome, Italy, Sept. 8-13. Dr. Armando Ferraro, 722 W. 168th St., New York, N. Y., U. S. A., Secretary General.

INTERNATIONAL CONGRESS OF OTO-NEURO-OPHTHALMOLOGY, Lisbon and Estoril, Portugal, April 22-26. Prof. Diogo Furtado, Servico de Neurologia, Hospital dos Capuchos, Lisbon, Portugal, General Secretary.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE, London, England, July 14-19. Dr. A. C. Boyle, 45, Lincoln's Inn Fields, London, W.C.2, England, Hon. Secretary.

INTERNATIONAL CONGRESS FOR THERMALISM AND CLIMATOTHALASSOTHERAPY, Nice-Cannes, France, April 3-8.

INTERNATIONAL SOCIETY OF GEOGRAPHIC PATHOLOGY, Liège, Belgium, July 15-18. Dr. Fred C. Roulet, Habelstr. 24, Basei, Switzerland, Secretary General.

INTERNATIONAL UNION AGAINST TUBERCULOSIS, Rio de Janeiro, Brazil, Aug. 24-27. Prof. Etienne Bernard, 66 Blvd. St. Michel, Paris 6^e, France, Secretary-General.

NEURORADIOLOGICAL SYMPOSIUM, Stockholm, Sweden, Sept. 17-20. Docent Ake Lindbom, Symposium Neuroradiologicum, Serafimerlasarettet, Stockholm K., Sweden, Secretary.

PAN-AMERICAN CONGRESS OF GASTROENTEROLOGY, Mexico City, D.F., May 11-17. Dr. R. Flores-Lopez, Calle Dr. Balmis, No. 148, Mexico City, D.F., Secretary.

PAN-EUROPEAN CONGRESS OF GASTROENTEROLOGY, Bologna, Florence and Rome, Italy, April 20-26. Prof. Guido Bassi, Policlinic of St. Orsola, Bologna, Italy, Secretary.

WORLD MEDICAL ASSOCIATION, Athens, Greece, Oct. 12-16. Dr. Louis H. Bauer, 2 East 103d St., New York 29, N. Y., Secretary General.

EXAMINATIONS AND LICENSURE

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Examination. Montgomery, June 24-26, 1952. Sec., Dr. D. G. Gill, 537 Dexter Ave., Montgomery 4.

ALASKA: Examination. Juneau, March 4. Also on application in other towns where there are board members. *Reciprocity*. On application. Sec., Dr. W. M. Whitehead, Box 140, Juneau.

ARIZONA: Examination. Phoenix, April 15-17. *Reciprocity*. Phoenix, April 19. Sec., Dr. J. H. Patterson, 316 W. McDowell St., Phoenix.

ARKANSAS: Examination. Regular. Little Rock, June 5-6. Sec., Dr. Joe Verser, Harrisburg, Homeopathic. Little Rock, June 10-11. Sec., Dr. Carl S. Bungart, 105 N. 14th St., Fort Smith. *Eclectic*. Little Rock, June 5-6. Sec., Dr. Frank C. Smith, 2301 Broadway, Little Rock.

CALIFORNIA: Written. Los Angeles, Feb. 18-21; San Francisco, June 23-26; Los Angeles, Aug. 18-21; Sacramento, Oct. 20-23. Application must be received at least two weeks prior to date of examination. *Oral for Reciprocity Applicants*. San Francisco, June 21; Los Angeles, Aug. 16; San Francisco, Nov. 8. Applicants are requested not to arrange to come to an oral examination until they receive notice from the *Credentials Committee*. *Oral and Clinical for Foreign Medical School Graduates*. San Francisco, June 22; Los Angeles, Aug. 17; San Francisco, Nov. 9. Sec., Dr. Frederick N. Scatena, 1028 N St., Sacramento.

COLORADO: Examination. Denver, June 10-12. Final date for filing application is May 12. *Reciprocity*. Denver, April 8. Final date for filing application is Mar. 10. Sec., Dr. Samuel H. Brown, 831 Republic Bldg., Denver.

CONNECTICUT: Regular Examination. Hartford, March 11-12. Sec. to the Board, Dr. Creighton Barker, 160 St. Ronan St., New Haven. Homeopathic Examination. Derby, March 11. Sec., Dr. Donald A. Davis, 38 Elizabeth St., Derby.

DELAWARE: Dover, July 8-10. Sec., Dr. Joseph S. McDaniel, 229 South State St., Dover.

DISTRICT OF COLUMBIA: Reciprocity. Washington, March 10. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Bldg., Washington.

FLORIDA: Examination. Jacksonville, June 29-July 1. Sec., Dr. Homer L. Pearson, 701 Dupont Bldg., Miami.

GEORGIA: Atlanta and Augusta, June. Sec., Mr. R. C. Coleman, 111 State Capital, Atlanta 3.

GUAM: The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Ex. Sec., Dr. Austin W. Matthis, Agaña.

IDAHO: Boise, July 14-16. Sec., Mr. Armand L. Bird, 305 Sun Bldg., Boise.

ILLINOIS: Examination. Chicago, April 1-3, June 24-26 and Oct. 7-9. Supt. of Regis., Mr. Charles F. Kervin, Capitol Bldg., Springfield.

INDIANA: Indianapolis, June 1952. Sec., Dr. Paul R. Tindall, 1138 K of P Bldg., Indianapolis 4.

IOWA: Examination. Iowa City, June 9-11. Sec., Dr. M. A. Royal, 506 Fleming Bldg., Des Moines.

KANSAS: Kansas City, June 4-5. Sec., Dr. O. W. Davidson, 864 New Brotherhood Bldg., Kansas City.

KENTUCKY: Examination. Louisville, June 4-6. Sec., Dr. Bruce Underwood, 620 S. Third St., Louisville.

MAINE: Portland, March 11-12. Sec., Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: Examination. Baltimore, June 17-20. Sec., Dr. Lewis P. Grundy, 1215 Cathedral St., Baltimore. Homeopathic. Baltimore, June 17-18. Sec., Dr. John A. Evans, 6029 Belfonta Ave., Baltimore.

MICHIGAN: Examination. June. Sec., Dr. J. E. McIntyre, 100 W. Allegan St., Lansing 8.

MINNESOTA: Minneapolis, April 15-17. Sec., Dr. Julian F. DuBois, 230 Lowry Medical Arts Bldg., St. Paul 2.

MONTANA: Helena, April 1. Sec., Dr. S. A. Cooney, 214 Power Block, Helena.

NEW HAMPSHIRE: Concord, March 12-13. Sec., Dr. John S. Wheeler, State House, Concord.

NEW JERSEY: Examination. Trenton, June 17-20. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, April 14-15. Sec., Dr. Charles J. McGoey, Coronado Bldg., Santa Fe.

NORTH CAROLINA: Reciprocity. Pinehurst, May 5. Written. Raleigh, June 16-19; Reciprocity. Raleigh, June 17. Sec., Dr. Joseph J. Combs, 716 Professional Bldg., Raleigh.

NORTH DAKOTA: Examination. Grand Forks, July 9-11. Reciprocity. Grand Forks, July 12. Sec., Dr. C. J. Glaspeil, Grafton.

OHIO: Examination. Columbus, June 17-20. Reciprocity. Columbus, April 1. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus 15.

OKLAHOMA: Examination. Oklahoma City, June 4-5. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON: Reciprocity. Portland, April 18-19. Examination. Portland, July. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland.

PUERTO RICO: Examination. San Juan, March 4. Sec., Mr. Luis Cueto Coll, Box 3717, Santurce.

RHODE ISLAND: Examination. Providence, April 3-4. Sec., Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: Reciprocity. Columbia, March 3 and April 7. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA: Rapid City, July 15. Sec., Dr. C. B. McVay, Yankton Clinic, Yankton.

TENNESSEE: Examination. Memphis, March 26-27. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis.

TEXAS: Fort Worth, June 19-21. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth.

UTAH: Examination. Salt Lake City, July. Asst. Dir., Mr. Frank E. Lees, 314 State Capitol Bldg., Salt Lake City 1.

VIRGINIA: Examination. Richmond, June 12-14. Reciprocity. Richmond, June 11. Sec., Dr. K. D. Graves, 631 First St., S.W., Roanoke.

VIRGIN ISLANDS: St. Thomas, June 4-5. Sec., Dr. Earle M. Rice, St. Thomas.

WEST VIRGINIA: Charleston, April 7-8. Sec., Dr. H. H. Dyer, State Office Bldg. No. 3, Charleston 5.

WASHINGTON: Seattle, July. Sec., Mr. Edward C. Dohm, Department of Licenses, Olympia.

WISCONSIN: Milwaukee, July 8-10. Sec., Dr. A. G. Koehler, 46 Washington Blvd., Oshkosh.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: Examination. On application. Juneau or other towns in Territory as decided by Board. *Reciprocity*. On application. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

ARIZONA: Tucson, March 18. Sec., Mr. Herbert D. Rhodes, University of Arizona, Tucson.

COLORADO: Denver, March 5-6. Examination. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

DISTRICT OF COLUMBIA: Examination. Washington, April 21-22. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Bldg., Washington, D. C.

FLORIDA: Gainesville, June 7. Examination. Sec., Mr. M. W. Emmel, Box 340, University of Florida, Gainesville.

OKLAHOMA: Examination. Oklahoma City, April 14. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON: Examination. Portland, March 1, June 7, Sept. 6 and Dec. 6. Sec., Dr. Charles D. Byrne, State Board of Higher Education, University of Oregon, Eugene.

TENNESSEE: Examination. Memphis and Nashville, March 20-21. Sec., Dr. O. W. Hyman, 874 Union Ave., Memphis.

TEXAS: Austin, April. Examination. Sec., Bro. Raphael Wilson, 306 Nalle Bldg., Austin.

WISCONSIN: Examination. Madison, April 5, and Milwaukee, June 7. Sec., Mr. W. H. Barber, Ripon College, Ripon.

* Basic Science Certificate required.

DEATHS

Du Puy, Howard Barham, Dallas, Texas; born in Tennessee Colony, Texas, Jan. 1, 1890; University of Texas School of Medicine, Galveston, 1917; member of the American Medical Association; fellow of the American College of Surgeons; during World War I, served as a first lieutenant in the Army Medical Corps; formerly on the faculty of Baylor University College of Medicine and Southwestern Medical School of the University of Texas; associate orthopedic surgeon, Dallas Medical and Surgical Clinic-Hospital; visiting surgeon, Baylor University Hospital; died Nov. 16, aged 61, of coronary occlusion.

Anderson, Hyrum Andrew, Rigby, Idaho; Harvard Medical School, Boston, 1896; member of the American Medical Association; before retirement served on the staff of the Idaho Falls Latter-Day Saints Hospital in Idaho Falls; died Dec. 29, aged 83, of chronic nephritis.

Anderson, James Vernie, Fort Worth, Texas; Loyola University School of Medicine, Chicago, 1916; affiliated with All Saints, Pennsylvania Avenue, and St. Joseph's hospitals; died Nov. 1, aged 61, of acute coronary occlusion.

Ball, John Dryer * Santa Ana, Calif.; University of California Medical School, San Francisco, 1922; member of the International College of Surgeons and the Industrial Medical Association; fellow of the American College of Surgeons; past president of the Western Association of Industrial Physicians and Surgeons; chief-of-staff, surgery, Orange County General Hospital in Orange; visiting surgeon, St. Joseph Hospital in Orange; died Dec. 20, aged 55, of coronary thrombosis.

Bellinger, Frank Earl * Council Bluffs, Iowa; John A. Creighton Medical College, Omaha, 1900; fellow of the American College of Surgeons; died Nov. 22, aged 77, of pneumonia and leukemia.

Casner, Andrew James * Bloomington, Ill.; Chicago College of Medicine and Surgery, 1909; past president of the McLean County Medical Society; served during World War I; on the staffs of the Mennonite and St. Joseph's hospitals; died Dec. 19, aged 74, of acute coronary thrombosis.

Decot, Valentine Alphonsis, Buffalo; University of Buffalo School of Medicine, 1904; member of the American Medical Association; served during World War I; chief-of-staff of the Sisters of Charity Hospital and consultant, department of Ophthalmology, Mercy Hospital; a director of the Genesee National Bank; in 1926 received an honorary LL.D. degree from Niagara University; died in Deaconess Hospital Dec. 19, aged 72, of arteriosclerotic heart disease.

Eggers, Gustave C., Two Rivers, Wis.; St. Louis College of Physicians and Surgeons, 1890; formerly practiced in Clayton, Mo., where for many years he was health commissioner of St. Louis County; died in St. John's Hospital, St. Louis, Dec. 20, aged 86.

Hash, Edward William * Chicago; Chicago Homeopathic Medical College, 1902; died in Oak Park Dec. 29, aged 82, of uremia, arteriosclerotic kidney disease, and diabetes mellitus.

Herrmann, Gustav J., St. Louis; Missouri Medical College, St. Louis, 1885; member of the American Medical Association; died in St. Louis Dec. 18, aged 89, of arteriosclerotic heart disease.

Hillman, Andrew Jackson, Ashland, Ky.; Hospital College of Medicine, Louisville, 1897; died in December, aged 81, of heart disease.

Karshner, Warner Melvin, Puyallup, Wash.; Northwestern University Medical School, Chicago, 1904; member of the American Medical Association; formerly state senator; fellow of the American College of Surgeons; at one time on the faculty of the University of Washington, Seattle; served on the staff of Puyallup General Hospital, where he died Dec. 19, aged 76, of hypertensive cardiovascular renal disease.

Lackey, Walter Adair, Oklahoma City; Vanderbilt University School of Medicine, Nashville, Tenn., 1892; died Dec. 21, aged 80, of a heart attack.

MacDowell, George Alonzo, Chicago; Rush Medical College, Chicago, 1896; member of the American Medical Association on the staff of Lutheran Deaconess Hospital; died Dec. 14, aged 79, of acute myocardial failure.

Mahre, John Alvin, St. Louis; University of Wisconsin Medical School, Madison, 1947; member of the American Medical Association and the Kansas Medical Society; assistant resident internal medicine on the staff of St. Louis City Hospital, where he died Dec. 30, aged 28, of carcinoma.

Mitchell, Samuel Robert * Milwaukee; Marquette University School of Medicine, Milwaukee, 1915; served during World War I; affiliated with St. Mary's Hospital, where he died Dec. 21, aged 65, of carcinoma.

Phelps, Robert May, Richmond, Ky.; Chicago Homeopathic Medical College, 1897; died Dec. 23, aged 76, of lob pneumonia.

Sloane, Joseph T., New York; Medico-Chirurgical College, Philadelphia, 1895; veteran of the Spanish-American War and World War I; died December 12, aged 81.

Smith, Grover Augustus * Montgomery, W. Va.; Medical College of Virginia, Richmond, 1915; for two terms was a member of the council of the state medical association; past president a secretary of the Fayette County Medical Society; served as member of the staff of Coal Valley Hospital, now known as Laird Memorial Hospital; died Dec. 26, aged 66, of heart disease.

Stoll, Karl Ludwig * Cincinnati; Ludwig-Maximilians-Universität Medizinische Fakultät, München, Bavaria, Germany, 1900; member of the American Academy of Ophthalmology and Otolaryngology; on the staff of the General Hospital and Deaconess Hospital, where he died Dec. 17, aged 76, of heart disease.

Sullivan, John J. * Reno, Nev.; Columbia University College of Physicians and Surgeons, New York, 1902; for many years chairman of the state board of health; formerly city health officer at one time regent of the University of Nevada; on the staff of St. Mary's Hospital; died Dec. 14, aged 74, of carcinoma.

Troxell, George Allen, Sarasota, Fla.; Baltimore Medical College, 1900; for many years practiced in Medfield, Mass., where was assistant superintendent until 1938 of the Medfield State Hospital; died December 14, aged 78, of arteriosclerosis and uremia.

Warfield, William Alonza, Washington, D. C.; Howard University College of Medicine, Washington, 1894; professor emeritus of abdominal surgery at his alma mater; for many years surgeon-in-chief of Freedmen's Hospital; died Dec. 18, aged 85, of cardiac failure.

Weber, Oliver Arkenburgh * Cleveland; Western Reserve University Medical Department, Cleveland, 1905; fellow of the American College of Surgeons; served on the faculty of his alma mater; affiliated with St. Vincent Charity Hospital and the Evangelical Deaconess Hospital; died December 16, aged 70, of cerebral hemorrhage.

Welton, William Archibald * Fairmont, W. Va.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1923; member of the Industrial Medical Association; fellow of the American College of Surgeons; served in France during World War I; affiliated with Fairmont General and Fairmont Emergency hospitals; died Dec. 19, aged 53, following an operation for brain tumor.

White, Harry J., Troy, N. Y.; Albany Medical College, 1890; member of the American Medical Association; served on the staff of Samaritan Hospital; died in the Albany (N. Y.) Hospital December 11, aged 73, of carcinomatosis.

* Indicates Fellow of the American Medical Association.

GOVERNMENT SERVICES

ARMY

Tribute to Army Research Team.—A research team from the Army Medical Service Graduate School, Washington, D. C., whose work demonstrated the value of chloramphenicol (chloromycetin®) in the prevention and control of scrub typhus and other infections, was given international recognition this month on receipt of a letter from the British ambassador to the secretary of state. The letter reads, in part:

"His Majesty's Ambassador for the United Kingdom presents his compliments to the Secretary of State and has the honour . . . to convey the thanks and appreciation of His Majesty's Government in the United Kingdom and of the Government of the Federation of Malaya for the work of the United States Army Medical Research unit which has been, since 1948, attached to the Institute for Medical Research at Kuala Lumpur.

"The work of this unit, under the leadership of Dr. Joseph A. Smadel and Lt. Col. Robert Traub, on a group of recently discovered drugs with a wide range of action on typhus, typhoid and other infections, has gained international regard. . . ."

Certified Specialists on Duty.—Five hundred officers now on active duty with the Army Medical Service have been certified as professional specialists, the Surgeon General, has announced. This number includes 466 physicians qualified in 19 medical specialties and subspecialties, 23 board-certified dentists, 7 specialists in psychology, and 4 in nutrition.

The current situation contrasts with that in 1945 when only 75 medical board specialists were on duty with the Army. Of the 500 specialists, 311 are regular Army Medical Corps officers, 148 are reserve or National Guard physicians on extended active duty and seven are retired regular Army officers remaining on active duty. When the Army began its residency training program five years ago, there were only 99 regular Army and 44 nonregular physicians with board certification on active duty.

In addition, 57 regular Army Medical Service Corps officers have received Ph.D. degrees and have had qualifying experience in fields such as entomology and sanitary engineering where specialty board certification is not possible. Many of the recently certified officers have obtained all their professional training and practice in the Army.

AIR FORCE

Commissions Available in Medical Services.—The Air Force has announced a program whereby commissions will be offered to young men and women practicing in all fields of medicine and in allied specialized vocations. The list of vocations includes doctors of preventive medicine, gastroenterologists, obstetricians, gynecologists, allergists, anesthesiologists, ophthalmologists, otorhinolaryngologists, neurologists, internists, general and orthopedic surgeons, radiologists, oral surgeons, periodontists, prosthodontists, medical supply and medical equipment maintenance specialists, sanitary engineers, clinical laboratory technicians, general duty and anesthetist nurses, dieticians, and physical therapists.

Each classification has a different set of requirements for each grade from second lieutenant through the higher grades. The First Air Force has set up clerical facilities for promptly answering all queries concerning these commissions. Inquiries should be directed to the Air Surgeon, Headquarters, First Air Force, Mitchel Air Force Base, New York.

Appoint Associate Editor.—The Surgeon General of the Air Force has nominated Col. Robert J. Benford as associate editor of the *U. S. Armed Forces Medical Journal*. Colonel Benford has specialized in the historical and bibliographical aspects of aviation medicine and is a member of the advisory editorial board for the *Journal of Aviation Medicine*. He is Air Force representative on the *Armed Forces Medical Journal* and on the consultants group for the Army Medical Library.

NAVY

Training Course in Amphibious Medicine.—The Bureau of Medicine and Surgery announces that a two week training course for Naval Reserve Medical and Dental officers in amphibious medicine will be conducted April 7-19, at the Naval Amphibious Base, Little Creek, Va. This course of instruction will familiarize inactive volunteer Naval Reserve Medical Department officers with amphibious operations and their medical aspects. It consists of lectures, training films, demonstrations, and practical exercises, and embarkation and debarkation phases of the medical service and the medical supply problems of an amphibious operation are dealt with.

Officers desiring this instruction should provide themselves with fatigue or utility type uniform equipment for participation in the practical aspects of the instructions. Meals and sleeping quarters will be available at the bachelor's officers quarters for officers who desire accommodations. Quotas for the course have been assigned to the commandants of the first, third, fourth, fifth, sixth, eighth, and ninth Naval Districts and the Potomac River Naval Command. Inactive volunteer reserve medical and dental officers residing in these districts who desire this course of instruction should request orders from the commandants of their Naval Districts. Active training duty orders in a pay status will be issued for this period of instruction.

The Legion of Merit Award.—Commander Thomas J. Canty, MC, in a recent ceremony at the Naval Hospital, Oakland, Calif., was presented the Legion of Merit for "exceptionally meritorious conduct in the performance of outstanding services to the Government of the United States as Chief of the Orthopedic Surgery; Officer-in-Charge of the Artificial Limb Department and Director of Prosthetic Research; Rehabilitation Officer at the United States Naval Hospital, Mare Island, California, from July 1945 to June 23, 1950." Commander Canty has remained as chief of the Navy's Amputee Center since it was moved to the Naval Hospital in Oakland in 1950 from the Mare Island Naval Hospital.

Reserve Consultants Board.—Dr. Benjamin Tenney Jr., professor of obstetrics and gynecology, Boston University School of Medicine, has accepted a position as reserve consultant to the Bureau of Medicine and Surgery to represent the specialty of obstetrics and gynecology. Dr. Tenney will fill the vacancy created in this group by the death last year of Dr. Paul Titus.

The Reserve Consultants Board of some 19 members meets in Washington, D. C., from time to time to advise the Bureau of Medicine and Surgery concerning matters pertaining to its graduate training program and to assist in the choice of reserve consultants to the staffs of naval hospitals and similar advisory duties.

Personal.—Dr. Howard T. Karsner, research advisor to the Surgeon General, was the guest speaker at the annual joint meeting of the Diplomates Association of Berks County Physicians and the Reading Eye, Ear, Nose, and Throat Society, Feb. 20, 1952, at Reading, Pa. The meeting was held jointly with the Southeastern Pennsylvania Chapter of the American College of Surgeons. Dr. Karsner's subject was "Modern Directions of Medical Investigation."—Capt. Frederick Ceres, MC, after more than 38 years continuous Naval service, was placed on the retired list on February 1. Captain Ceres in 1939 organized and founded the Naval School of Aviation Medicine, Pensacola, Fla.—Capt. John Ryer Poppen, MC, retired after nearly 36 years of active Navy duty January 1. Prior to retirement he had served as director of the Navy's newest aviation medical acceleration laboratory at Johnsville, Bucks County, Pa.—Rear Adm. Lamont Pugh, Surgeon General, was honored December 1, 1951, in ceremonies at Wagner College, Staten Island, N. Y., when the college bestowed on him an honorary degree of Doctor of Laws.

FOREIGN LETTERS

BRAZIL

Chagas' Disease.—Chagas' disease, or schizotrypanosis, is now well known in many aspects. Searches have been carried out, based on findings of complement fixation tests and xenodiagnoses, to determine the extent of Chagas' disease in Central Brazil.

Pedreira de Freitas, working in rural regions of São Paulo and Minas, obtained 511 positive tests from 996 serums, that is, 51.3%. Using the same tests in soldiers of the second military region, Faria and his co-workers found 41 positive reactions from 141 serums (29.07%). Miron de Menezes found a positive reaction in 32 cases out of 59 at his cardiology clinic in Uberlândia (54.2%). In the capital of Minas, Pellegrino and Borotchin found 37 positive reactions among 181 nonselected patients in Santa Casa Hospital (20.4%). In Uberaba, Rubem Jacomo got, from 226 tests, 119 positive results (52.6%). From a total of 2,893 tests performed in Minas, São Paulo, and Goiaz, 52.5% show a positive result, revealing the high incidence of schizotrypanosis in these regions of Central Brazil.

The significance of Chagas' infection should be considered as an important factor of the poor health of the rural population, one that reduces their productive capacity. Since the basic work of Chagas, Gaspar Vianna, and Margarinos Torres, the affinity of *Schizotrypanos cruzi* for the heart has been well known. The contracting fibers are invaded by multiplying forms of *Leishmania*, which cause acute myocarditis, at times of such intensity, according to Torres, as is not equalled by any other disease process in human pathology. The well-known classical works of Chagas, Vilela, and Evandro Chagas, describe the clinical manifestations of Chagas' cardiopathy, the multiple alterations of rhythm, which reveal the myocardial lesions due to the parasitic invasion.

Thus, in 208 cases of chronic Chagas' cardiopathy studied in Bambui, it was found that 155, or 74.3%, showed alterations in conduction, among which right bundle branch block (43.3%) and auriculoventricular block (30.3%) predominate. As for disturbances in stimulus formation, ventricular extrasystoles stand out, occurring in at least 52.9% of the cases. The most serious finding is, however, that the electrocardiographic alterations indicative of myocardial lesion were found in about 50% of the cases of chronic schizotrypanosis in that region. The idea is thus confirmed that, at least in Brazil, Chagas' disease is essentially a cardiotropic infection, as pointed out by Dr. Emmanuel Dias, of Instituto Oswaldo Cruz.

Ethnic Aspects of Portal Vein.—Anatomic observations on the confluence of the "roots" of the portal vein in whites, Negroes, and mulattoes were performed by Dr. Liberato Di Dio at the anatomy department of the Faculdade de Medicina de São Paulo. He studied the confluence of the roots of the portal vein in 191 cadavers (94 whites, 62 men and 32 women; 59 Negroes, 37 men and 22 women; and 38 mulattoes, 27 men and 11 women). Dr. Di Dio's conclusions are as follows.

1. The most frequent disposition, 92.1%, is the "biradicular portal vein," in which the inferior mesenteric vein ends either in the splenic (A biradicular type [47.1%]) or in the superior mesenteric vein (B biradicular type [45%]) without ethnic difference.

2. Of the cadavers, 7.9% have the confluence of the three veins: superior and inferior mesenteric and splenic constituting the trunk of the portal vein (triradicular type).

3. Among the whites, the incidence of cases in which the inferior mesenteric vein ended in the splenic vein was 58.1% greater in the men than in the women (28.1%). The incidence of cases in which the inferior mesenteric vein ended in the superior vein was 62.5% greater in women than in the males (35.5%). In the Negroes and mulattoes there was no sex difference in the incidence of these conditions.

LONDON

National Health Service Charges.—Details of the charges that the government proposes to impose in the National Health Service, as part of the plan to deal with the present economic emergency, have now been announced. The total effect will be to save £20 million a year on the service. A charge of 1s. will be made on each prescription form issued, although the form may contain more than one prescription. This will apply to prescriptions issued by physicians and dentists and prescriptions issued to hospital outpatients. Patients receiving national assistance, or their dependents, will be able to reclaim this sum. It is estimated that these charges will bring in £12 million a year from general prescriptions and £500,000 from hospital prescriptions. A fixed flat rate charge representing about half the cost will be made for certain appliances supplied to hospital outpatients; these will include surgical belts and boots, hearing aids, wigs, and the full cost of repairing of these appliances. No charge will be made for these appliances when they are supplied to hospital inpatients or to outpatients who are under 16 years of age or in full-time attendance at school, recipients of national assistance or their dependents, or war pensioners, if the appliance is supplied because of an accepted pensionable disability. This charge, it is estimated will save £500,000 a year. Charges ranging from 5s. to 10s. will be made for elastic hosiery prescribed by general practitioners. The charge for "amenity" beds in hospitals will be doubled, and a charge of £1 (or the full cost, if less) will be made for all dental treatment except dentures, for which the patient is already charged. This will not apply to children under the age of 16, persons who are in full-time attendance at school, expectant or nursing mothers, or dental patients who are treated in a hospital. The charges will bring in £7,500,000 a year.

The passage of these new regulations through Parliament is expected to result in heated controversy. As for the medical profession, the consensus of opinion is that the service must share in the cuts imposed by the present financial stringency; one of the major effects of the charges will be on reducing the number of unnecessary calls made by patients on their physicians.

Spiritual Healing.—There has been a renewal of interest in spiritual healing in England since the end of World War II, and, during its recent session, the Lower House of Convocation, of the Church of England, approved a motion "That this House commends to the sympathetic attention of the Church and particularly of parish priests the modern revival of spiritual healing" and asked the Archbishop of Canterbury to appoint a committee "to examine the problems and opportunities raised by the modern revival of spiritual healing and report." In introducing the motion, the Dean of Salisbury took the view that one of the principal causes of the present drift from religion was the number of unorthodox sects, which, on a false theological basis, claimed to make up for what they thought was lacking in the Church in its attitude toward healing. He claimed that a revival of spiritual healing would do much to set the balance right. During the subsequent debate, it was emphasized that spiritual healing was not in competition with medical science, and that, in recent years, orthodox workers had come to recognize the value of spiritual factors. Appeals were made for increasing cooperation between physicians and priests.

This debate has drawn attention to the work of the Guild of Health that has over 50 years of research and experience behind it; through its long tradition of collaboration with the medical profession, the guild has avoided many of the pitfalls into which spiritual healers so often fall. The guild has just established a center, the main purpose of which is "to enable clergy, doctors, psychologists, and members of the nursing profession to work together in furthering the cause of health and healing." The work of the center is threefold, therapy, reeducation, and research. It is interdenominational and has the support of the leading representatives of the Church of England and the free churches.

annual Toll of Burns and Scalds.—In an article in *The Times*, r. Leonard Colebrook, former director of the Medical Research Council, Burns Unit, discusses a subject that he has studied intensively during recent years, the toll of life and disability caused by burns and scalds. The death rate from these accidents in England is 14 per 1,000,000, compared with 55 per 1,000,000 in the United States (in 1948), and 10 per 1,000,000 in Sweden (in 1947). The incidence of nonfatal accidents is much higher, and it is calculated that 15,000 to 20,000 burn and scald patients are admitted to hospitals every year in England and Wales and that 50,000 more are treated as outpatients. The average stay in the hospital is 40 to 50 days, and these patients occupy hospital beds for at least 857,000 days. An extensive six-year study, recently completed in Birmingham population, 1,000,000, showed that production time lost by such injuries to adults between the ages of 15 and 64 years was 1,000 days a year, and that, among children aged 5 to 14 years, schooling loss amounted to 6,000 days a year. Of the 2,000 consecutive accidents studied, two-thirds occurred in the home, and one-half of these cases were scalds, and 80% of the victims were children. The other half, which included practically all the fatalities and crippling injuries, were burns that were caused by guarded fires and the high inflammability of the clothing material worn by women and girls. The open coal fire, "the standing hazard of the English home," was responsible for 5 of the 724 home burns, which included 35 deaths. Gas and electric fires were responsible for 144 cases (80% were old persons and children), which included 20 deaths. Prevention consists of a more intensive search for nonflammable fabrics that are both aesthetically pleasing and reasonably priced and guarding of fires. In the case of coal fires, new types of fire-ards are being experimented with, and it is hoped that when these are available, local authorities will loan them or sell them at cost price to persons with homes in which there are old persons or children. The sale of gas and electric fire apparatus could be forbidden unless they are adequately guarded. As a long-term solution "the development of central and district heating and the better insulation of houses (making fires less often necessary)" are recommended.

beds in Hospital.—In a featured article in the *Times* is discussed a problem that is giving rise to much anxiety at the moment—the inability of the new hospital service to afford the reasonable measure of privacy wanted or needed by some patients. As the result of a recent investigation, the Nuffield Trust concludes that a quarter of all beds in medical and surgical wards could be placed in single rooms, in order to accommodate those patients for whom such privacy is necessary on medical grounds, e.g., those who are dying, infectious, and distressed by, or distressing to, other patients. The *Times* correspondent suggests that this allocation "would commonly leave some margin for patients with a personal preference, as distinct from a medical need, for separation." In order to find out whether this allocation would be effected without any increase in cost or staff, experimental wards are being built. Even if this experiment is successful, it will be many years before the plan can be generally accepted, as the hospitals of this country were designed and built to house patients in large open wards. Under the National Health Service, beds in single rooms or small wards, if not required for patients needing isolation on medical grounds, can be used by patients seeking privacy for personal reasons at a weekly fee of 42 shillings for a single room and 21 shillings for a bed in a shared room. In England and Wales these "amenity beds" have seldom been used for this purpose, and the bulk of those that have been used for this purpose have been in mental hospitals. In Scotland they have been used to a much greater extent for patients desiring privacy on personal grounds. For instance, while Scotland has a quarter of all the nation's "amenity beds," it earns nearly half of all the fees paid, averaging £63 a year for each bed as against £8 in the English teaching hospitals and 14 in English nonteaching hospitals. As the *Times* points out, if the existence of amenity beds were not so generally concealed from patients south of the border, the Scottish example suggests that the health service could double the small income from fees for amenity beds without raising the charge or increasing the number of such beds."

An alternative method whereby patients can obtain privacy is to use one of the 7,600 private pay-beds, "which are still reserved largely for patients outside the health service who personally pay both physicians and hospitals for services given." Over a quarter of these beds are in teaching hospitals. These pay-beds in hospitals were originally provided in order to help private patients who were unable to pay the fees of private nursing homes. Gradually, however, the charges for them tended to be raised, as the hospitals found them a useful source of income, and in many cases they reached a level that the ordinary private middle-class patient could not afford. This process was accentuated with the advent of the National Health Service, which abolished the subsidized private pay-bed and insisted that the charges for such private beds in hospitals should meet their full cost. These costs have now reached such a level that relatively few patients can afford them, and the demand for such beds is falling. To some this would appear not unreasonable, and they would contend that these private pay-beds could be put to a much better use, e.g., to cut down the waiting list of tuberculous patients. The *Times* contends that "public opinion would not tolerate the complete exclusion from the public hospitals of patients who, while deliberately preferring to choose and personally pay their own physicians or surgeons, require treatment of a kind not possible in even the best-equipped private institution."

The *Times'* article rejects the British Medical Association's solution of the problem, that amenity beds should be converted into pay-beds and that the charge for these should be subsidized by the service. As an alternative, it suggests that half the present unsubsidized beds be kept for patients who can afford to pay the full charge, that the other half be converted into amenity beds, and that the charge for all amenity beds be raised to from £3 to £6. This would increase the hospitals' income, would insure that the beds were all occupied, and would provide some measure of relief to that most harassed section of the whole community at the present—the middle or professional class.

The Law and the Illegitimate Child.—A joint committee of the British Medical Association and the Magistrates' Association has issued a report entitled "The Law in Relation to the Illegitimate Child." This has received the unanimous approval of the Council of the British Medical Association, but the Council of the Magistrates' Association, although agreeing to publication, does not accept all the views expressed. The committee decided that "the law concerning the maintenance, custody, and welfare of illegitimate children is in urgent need of revision" and recommends that a committee of inquiry be set up by the government to investigate the problem. The following recommendations are among the more important conclusions reached by the committee.

It asks for investigation of the present rule that a child cannot become legitimate on the subsequent marriage of the parents, if one of the parents was married to a third person when the child was born. At present, the maximum payment that can be ordered by a Magistrates' court for the maintenance of an illegitimate child is £1 a week, whereas in the case of a child born in wedlock, it is 30s. It is recommended that the payment for an illegitimate child be equal to that for a legitimate child. The present law, whereby procedures to enforce payment on a bastardy order cannot be taken after the death of the father, should be amended. It is considered that marriage of the parents should not automatically be regarded as the solution to the problem of the illegitimate child. If there be no evidence to the contrary, an illegitimate child should remain with the mother, but, in exceptional cases, a court should be able to grant custody to the father. "As far as possible, every illegitimate child should be brought up in a home and a family" and should only be sent to an institution after all else fails. The committee considers that it is "usually wiser" to disclose the fact of its illegitimacy to a child "because it almost inevitably finds out sooner or later, with the consequent risk of grave psychological damage." It is recommended that the child's legitimacy be explained "at an age when the child can understand the implications, say, between eight and 11 years of age, or earlier in response to questions from the child." The child should not be told of its illegitimacy during

adolescence "unless the case has first been referred for expert advice." A new name for the illegitimate child is desirable. The terms "illegitimate child" and "bastard" are undesirable, and, although a satisfactory substitute could not be agreed on, it was felt that of the suggested names, "natural child" was the least objectionable.

NORWAY

Old Age Research.—When the influential Norwegian National Association Against Tuberculosis recently changed its title to the National Association Against Tuberculosis and for Health, it wished to stress the interest it intended to take in other fields in addition to tuberculosis. One of its most recent activities is concerned with old age. It has appointed a committee with the title of the Health Committee of the Old. Its chairman is Dr. Per Hanssen, head of the medical department of a public hospital in Stavanger. In an address on geriatric problems, delivered at a postgraduate course for doctors, he emphasized the importance and size of the problem of old age by quoting figures published by the Norwegian Statistical Central Bureau, concerning the increase in the expectation of life in Norway. According to this source of information, which dealt with the two periods 1931-1940 and 1945-1948, there was such a remarkable increase between these two periods in the expectation of life that the man who was 80 in the former period could hope to live another 5.8 years, whereas in the latter period his expectation of life would be raised to 6.4 years. This remarkable achievement in a short time may be a tribute to the more effective control of certain infectious diseases by the sulphonamides and the antibiotics, but it is also a reminder that the ranks of the aged are being recruited at a rapidly increasing rate. By the same token the responsibilities of youth are being enormously increased.

Dr. Hanssen pointed out that the association includes in its program stimulation of scientific research into health problems of the aged. The committee is to devise a plan of research with reference to the different needs of the aged, according to whether they live in town, in the country, or in different parts of Norway where the conditions of life are not uniform. The committee is also to inquire into the mental attitude of the aged towards their environment, into the diseases to which they are peculiarly liable, and into the diet most suitable for them. They are to be asked whether they are satisfied with retirement or would prefer daily occupation and duties. With the cooperation of the medical profession, it is hoped that much useful information will soon be collected on this subject.

Tuberculosis Depending on Intensity of Infection.—For nearly three decades Dr. J. Heimbeck has carried out tuberculin and BCG vaccine studies of nurses at the Ullevaal Hospital and of other groups of persons. He has come to the conclusion that in many cases the development of tuberculosis depends on the intensity with which infection occurs. In support of this opinion he has published in the organ of the Norwegian Medical Association, *Tidsskrift for den norske lægeforening*, for Jan. 1, a statistical investigation covering a wide field over a long period. One of his statistical tables deals with 253 Ullevaal nurses who, between 1924 and 1936, were exposed to intensive infection in the course of nursing. They were originally Pirquet negative, and they were not vaccinated with BCG. In this group there was a tuberculosis morbidity of 43% and a tuberculosis mortality of 5.5%. Serving as a control group were 948 young women of the same age, living in Oslo, who were originally Pirquet negative. They were no more exposed to infection with tuberculosis than other members of the community. In the course of more than 5,000 observation years, 250 of these women became infected with tuberculosis, 51 of them developing definite tuberculosis and 5 of them dying of it. There was a tuberculosis morbidity of 20% and a tuberculosis mortality of 2%. In other words, the tuberculosis morbidity and mortality were twice as high among the nurses as in the controlled group.

Another comparison concerned 668 Pirquet-positive probationer nurses who, in the course of three years of nursing and exposed to intensive infection, showed a tuberculosis morbidity

of 11.3 and a tuberculosis mortality of 0.5 per 1,000 observation years. Serving as controlled persons were 620 nurses kept under observation after their completion of training as nurses. Nearly all of them had ceased to be exposed to intensive infection with the result, according to Dr. Heimbeck, that they showed a tuberculosis morbidity of only 2.2 per 1,000 observation years, i. e., a tuberculosis morbidity of only one-fifth of that of the nurses in attendance on infectious cases. In another statistical comparison, Dr. Heimbeck believes that after vaccination with BCG the prospect of developing tuberculosis depends largely on whether the persons concerned are or are not exposed to intensive infection. He argues that intensity of infection is of great importance not only to a primary infection but also to superinfections and that for this reason tuberculosis patients may suffer from contacts with their fellow patients.

A New Institute for Experimental Medical Research.—Last December the new institute for experimental medical research at the Ullevaal Hospital (Oslo City Hospital) was formally opened. It is the first institute of its kind in Norway, and it is the outcome of much generous enterprise. Earlier last year whale oil interests made a gift of one million kroner to the University of Oslo, with a view to the establishment of a research institute. Later in the year another contribution of 350,000 kroner was made by Anders Jahre, one of the leaders of the whale oil industry. Another sum of 200,000 kroner, to be spent at the rate of 40,000 kroner a year for five years, has also been contributed. These sums are administered by a university committee, whose chairman is Prof. Carl Semb. At the institute's headquarters, Dr. A. Kolberg is already engaged on research into the physiology of the kidneys. Working as technical assistant is Mary Frances Morrill of the Massachusetts General Hospital. The institute is advertising a vacancy for a young doctor with an inclination for research into the peripheral circulatory system. A minimum salary of 12,000 kroner a year will be available for three years. The holder of this appointment will be given financial support for preliminary studies at home and abroad before he takes up his new duties.

PARIS

Bronchiectatic Aspergilloma.—On Oct. 16, 1951, O. Monod, G. Pesle, and G. Ségretain discussed, before the National Academy of Medicine, a new form of pulmonary aspergilloma, caused by *Aspergillus fumigatus*, which they propose to name bronchiectatic aspergilloma. Three cases were diagnosed by the authors, two by Professor Orié, and four were found in the medical literature under various appellations. This new pathological entity is characterized by a spherical mycelian tumor (consisting of the entanglement of ramified filaments) enclosed in a bronchial cavity. It is located in the floor of a smooth, regular cavity; there are two bronchial apertures, thus presenting a sacciform ectasia. The reaction of the neighboring bronchial tissue suggests a basic action of the fungus, which, nevertheless, does not penetrate deeply into the pulmonary tissues. Contrarily to parasitosis or bronchopulmonary tumors, the lesion is not inflammatory; the authors are inclined to think that this fungus forms an antibiotic. Another phenomenon, unusual in pulmonary pathology, is the absence of bronchial obstruction, atelectasis, and suppuration. The diagnosis depends on the strikingly characteristic radiographic picture, which, in all nine patients, was able to be superimposed. It presented a uniform, slightly dense opacity, was rounded, or in the form of an almond, and surmounted with a clear, thin crescent surrounding its superior three quarters; in two patients, followed for five and six years, roentgen appearances remained unchanged. The culture from sputum and from the product of the exploratory puncture confirmed the diagnosis. Clinically, bronchiectatic aspergilloma is manifested by hemoptysis of red blood for months and years.

Treatment.—The only effective treatment of this chronic disease is segmental exeresis, which removes the lesion and preserves the rest of the lung; iodine, antibiotics, or radiotherapy were ineffective.

CORRESPONDENCE

FOREIGN BODY IN THE EYE

To the Editor:—An article entitled "Simple Removal of Ocular Foreign Bodies," on page 119 of the Jan. 12, 1952, issue of *THE JOURNAL* states that a BB shot was in the center of the vitreous and "that with pressure applied over the most posterior aspects of the visible sclera the BB popped out of the eyeball with a yellow gelatinous material that took the form of a long tail." Any competent ophthalmologist will quickly recognize this as conjunctival secretion. The foreign body never was inside of the globe but only in the conjunctival sac, and when the lids were opened the shot fell out. The report is clinically misleading and may be also dangerous, for it recommends a method of treatment fraught with grave risks.

The reporter failed to find any opening in the globe before or even after his manual expression. This is sufficient to cast a deep shadow of doubt regarding the primary observation and discredits the secondary deductions and recommendations, for, if the shot had been inside of the eye, there would have been a visible hole in the globe after its extrusion.

All physicians should avoid pressure on the eyeball as a means of removing an intraocular foreign body. Each case is a law unto itself and should have the best possible expert care. Disregard of this admonition will lead to serious disaster and a disheartening outcome.

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344 State St., Albany, N. Y.

HYPOCOAGULABILITY OF IRRADIATED PLASMAS

To the Editor:—Our paper on "Hypocoagulability of Certain Irradiated Plasmas," in *THE JOURNAL*, July 22, 1950, page 1057, has provoked a "reinvestigation" of our work by Kaplan and Friedman ("Effects of Ultraviolet-Ray Irradiation on Clotting Mechanism of Plasma," *J. A. M. A.* 147:229 [Sept. 15] 1951), in which they conclude that our ideas are erroneous and our conclusions untenable. We wish now to compare our original statements and the data of Kaplan and Friedman, which supposedly refute our findings.

We examined the coagulability of various lots of human plasmas, irradiated, unirradiated, fresh, lyophilized, and plasma stored in liquid form. Irradiated liquid plasma, prepared and distributed by the Michael Reese Research Foundation, could not be coagulated by thrombin, even when applied in great concentrations. We stated that this phenomenon is due to the effect of ultraviolet irradiation. Kaplan and Friedman challenge this statement and set up two experiments to determine the effect, if any, of ultraviolet irradiation on fresh and on three-month-old liquid plasma, with results as shown in their tables 1 and 2 respectively. In table 1, we find but a single comparison. Here they compare the clotting time (after addition of thrombin) of a single four-day-old plasma sample before and after irradiation. Under the heading Conclusions, they state, "The ultraviolet-ray irradiation of fresh plasma does not alter its clotting mechanism." Under Comment they state, "... the clotting of fresh irradiated plasma is practically the same as that of an aliquot unirradiated sample." Under the heading Results, they state, "The results show the clotting mechanism of the irradiated plasma to be identical with the aliquot unirradiated sample and the control sample." These statements are specific but are not in accord with the facts given in their first table. The clotting time after irradiation rose from 29 to 35 seconds, an increase of 20.7%! The second table is equally interesting; here the clotting time of eight pools of three-month-old liquid plasma are again compared before and after irradiation. At this point Kaplan and Friedman admit that, in this experiment, "the procedure of ultraviolet-ray

irradiation does alter the clotting mechanism," but they attempt to minimize the effect of this admission by stating, "This alteration is of the magnitude of fractions of a minute." What are the facts given in their second table? After irradiation, the clotting time (after addition of 1 unit of thrombin) rose sharply in every instance. The average increase was 44.2%, and the greatest increase was 71.0%! If, in their second table, we further compare the postirradiation clotting times as measured by 40 units of thrombin plus 1 mg. of heparin, the changes are even more spectacular: an average rise of 119%, and a maximum rise of 200%! We thus see the confirmation of our claim that ultraviolet irradiation alters the coagulability of plasma.

The second part of our paper described our demonstration that this failure of irradiated liquid plasma to clot could be substantially reversed by addition of protamine sulfate or of toluidine blue. We gave data indicating that an inverse ratio exists between the amounts of thrombin, on the one hand, and of protamine or toluidine, on the other hand, needed to clot the seemingly incoagulable Michael Reese plasma. As a control mixture of protamine, thrombin, and serum or defibrinated plasma does not clot, we thus demonstrate, conclusively, the presence in the irradiated and aged liquid plasma of fibrinogen in amounts adequate for clot formation. Kaplan and Friedman do not comment on this vital point, and nowhere in their paper is there mention of any attempt to confirm or deny this finding. This is indeed a serious omission in a study whose entire purpose is a "reinvestigation" of our work.

What explanation for our findings do Kaplan and Friedman offer? We quote from their conclusions: "The inability of aged liquid plasma to clot upon the addition of thrombin is due to the disappearance of fibrinogen" As we had already proved the presence of fibrinogen, it is interesting to seek the evidence Kaplan and Friedman use to deduce its absence. They do not present one direct analysis for fibrinogen in even a single sample of plasma; however, by citing the careful studies of Taylor and associates (*J. Clin. Invest.* 23:351 [May] 1944) Kaplan and Friedman leave the erroneous impression that these workers are responsible for the following statement: "By the end of six months, the prothrombin level is down to 2%, and the fibrinogen has completely disappeared." Actually, Taylor and his co-workers were fully aware of the deterioration of the coagulation mechanism, and, after carefully describing their methods for determining fibrinogen, state, in reference to liquid plasma stored over a period of six months, "Fibrinogen, when it was possible to determine it, was present in normal amounts. As is shown in the protocol, fibrinogen could not be determined in the older liquid plasmas due to failure of the coagulation mechanism. The clotting properties, when thrombin was used were likewise impaired in some instances." Kaplan and Friedman then show, in their third table, that unirradiated aged plasma fails to clot. This is, of course, well known, having been demonstrated by Taylor in 1944, and, in any event, is no confirmation of the alleged absence of fibrinogen. Finally, in an effort to prove the absence of fibrinogen in the aged plasmas, Kaplan and Friedman add fresh fibrinogen to a variety of mixtures containing thrombin and produce clots. From this they conclude that they have replaced the missing fibrinogen but fail to recognize that the addition of sufficient fibrinogen and thrombin to any fluid produces fibrin clots. Thus this experiment proves nothing about the fibrinogen content of the original fluid.

The remainder of Kaplan and Friedman's paper attempts to explain our third finding, that of the anticoagulant properties of irradiated (or aged) plasmas. We quote from our paper: "It was then found that this failure to clot held, in mixtures of M. R. [Michael Reese] B. B. [Blood Bank] plasma: 0.5

sodium chloride solution plus 0.5 units thrombin clotted; 0.5 cc. B. B. plasma plus 0.5 cc. M. R. plasma plus 0.5 units thrombin did not clot. This latter mixture required 4 units of thrombin to clot, representing an eight to tenfold increase over the amount of thrombin required to clot the control plasma." Apparently, in attempting to test this finding, Kaplan and Friedman kept their thrombin constant, adding fibrinogen, and found that an unexpectedly large amount of fibrinogen was needed for clot formation. One thus sees that the irradiated or aged plasmas contain an anticoagulant that prevents the action of thrombin on fibrinogen, until a large excess of fresh fibrinogen is added. Although our explanation is rejected, Kaplan and Friedman offer no alternative theory, merely stating that "changes other than those already noted occur in aging plasma." At this point in the discussion of our paper, results given in our table 3 are erroneously interpolated, quite out of context, instead of results from a similar table illustrating in greater detail our findings quoted immediately above. As things stand, Kaplan and Friedman are quite correct in attributing the results seen in our table 3 to excess oxalate effect; however, oxalate obviously plays no part in any of the mechanisms discussed thus far, as the action of thrombin on fibrinogen occurs at a later stage in the clotting mechanism than the stage at which calcium ions are needed. This is self-evident. The final table in Kaplan and Friedman's paper demonstrates that five recipients were unharmed by the infusion of 600 cc. of irradiated liquid plasma. No details are given, but if the subjects are adults, they would probably have sufficient circulating and stored fibrinogen to escape hemorrhagic complications. It would be prudent to perform similar experiments cautiously.

We therefore find that, although Kaplan and Friedman differ with us, their own data clearly support our conclusions.

A recent study by Lyttleton and Vallet, "Coagulability of Irradiated Plasma," (*Lancet* 1:1102 [May 19] 1951) confirms our finding that ultraviolet irradiation of plasma markedly prolongs the clotting time. In a careful series of experiments, Lyttleton and Vallet exclude the effect of mechanical agitation or of ozone, and demonstrate that purified fibrinogen itself undergoes changes after irradiation that are clearly responsible for the changes in irradiated plasma. Shinowara (*Federation Proc.* 10:246 [March] 1951) tested dried human plasma stored four to six years and found adequate amounts of fibrinogen, prothrombin, and thromboplastic plasma component (TPC). After ultraviolet irradiation, marked decrease of TPC was noted. Shinowara therefore warns, "Presently available plasma treated with ultraviolet radiation to destroy possible viral and bacterial contaminants would be of questionable value for a hemophiliac or any individual whose hemorrhage is due to TPC deficiency."

Finally, we wish to comment, briefly, on the electrophoretic patterns of irradiated plasma. The Michael Reese group states (in package literature distributed with their plasma) that, following ultraviolet irradiation, "Electrophoretic studies showed no change in pattern or mobility of the proteins," and again, apparently referring to the same source (Wolf, and others: *J. A. M. A.* 135:476 [Oct. 25] 1947): "There were no consistent variations between irradiated and nonirradiated samples." This lack of change, if true, would be most surprising, in the face of the well-known ability of ultraviolet energy to denature proteins. Compare, for example, Davis, Hollaender, and Greenstein (*J. Biol. Chem.* 146:663 [Dec.] 1942) where, following heavy ultraviolet irradiation, denaturation of plasma proteins was clearly shown by changes in the electrophoretic pattern, colloid osmotic pressure, and viscosity. To clarify these conflicting statements, we submitted different samples of unirradiated pooled liquid plasma and Michael Reese plasma (irradiated and aged liquid plasma) to an outstanding expert in electrophoresis, Dr. Kurt G. Stern. We quote, with permission, from his detailed report: "The Michael Reese material exhibits a highly anomalous electrophoretic pattern. The changes here found far exceed any changes we have observed on storage, and the plasma here must be considered a modified or derivative protein spectrum, rather than one representative of native human plasma. From the dia-

grams obtained, the presence of *unmodified* fibrinogen and *unmodified* gamma globulin can be excluded, which in itself would explain the abnormal clotting properties of the plasma." Thus, our finding that ultraviolet irradiation of plasma causes alteration of the clotting mechanism is further substantiated.

The following conclusions seem warranted:

1. Ultraviolet irradiation of fresh or moderately aged liquid plasma markedly impairs its coagulability. As stale liquid plasma has already deteriorated to the point of incoagulability, it is at present not known what further effects ultraviolet irradiation may have. (We are now attacking this problem by studies of the length of the fibrinogen molecule.)

2. Anticoagulant effects of these plasmas when mixed with normal blood or plasma are clearly demonstrable. Inasmuch as this effect is revealed with the use of preformed thrombin, the first and second stages of coagulation are not involved, and the action of thromboplastin, ac-globulin, calcium ions, or oxalate need not be considered.

3. Irradiated plasma stored in the liquid state bears little resemblance to unprocessed human plasma, and is of value principally for its osmotic properties, as are polyvinyl pyrrolidone, dextrans, and similar substitutes. This plasma should not be given to persons exposed to ionizing radiation from atomic bomb or other sources. It should be used in hemorrhagic shock and in bleeding diatheses only when whole blood, fresh plasma, or lyophilized plasma is not available. Because of the "derivative," (denatured?) protein present, one would use this material with more confidence if appropriate investigations of the long-term effects of this protein upon the liver, the kidney, and the reticuloendothelial system demonstrated its harmlessness.

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BLOOD COAGULATION

To the Editor:—The recent article "Influence of Some Drugs and of Emotions on Blood Coagulations," by Dr. D. I. Macht, in *THE JOURNAL* (148:265 [Jan. 26] 1952) ascribes to several common drugs an important influence in increasing blood coagulability and associates this effect with thrombotic and embolic episodes in patients receiving these drugs. Some negative views were cited but a more reliable conclusion would be reached if still others, such as the following, were examined. Sutton, Levin and Ruskin, Sokoloff and Ferrer, Moses, Poindexter and Meyers, and Fowler have examined the possible effect of digitaloids on the blood clotting mechanism in patients. Each of these studies demonstrated that the usual variations in such factors as clotting time and prothrombin time are not significantly changed after digitalization. Similarly, Fahey found that corticotropin and cortisone had no significant effect on coagulability of whole blood in patients with and without adrenal syndromes. Shapse and Wright and Lasser, Versakos, and Loewe reported that aureomycin had no effect on blood clotting in patients. Poindexter and Meyers reported that morphine, mercurphyllin injection (mercupurin®), and several other common drugs had no apparent effect on prothrombin clotting time in patients. Moses found that epinephrine produced no significant effects on heparin tolerance curves in patients, and Wakim, Fink, and Chen found epinephrine did not significantly influence prothrombin clotting time of animals. None of these reports were cited in the article mentioned above. Hines and Kessler were quoted as finding thromboplastic effects following administration of penicillin. Actually, they reported penicillin either had no effect on prothrombin time or appeared to potentiate the anticoagulant effects of heparin in a few patients. Other uncited negative reports of this type have appeared, some of which have been quoted recently by Marple and Wright.

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COUNCIL ON MEDICAL SERVICE

PROGRESS REPORT ON GRIEVANCE COMMITTEES

A little more than two years ago, in December, 1949, the House of Delegates of the American Medical Association adopted a resolution urging that all constituent medical associations have committees to hear complaints from the public. All state medical associations have for a long time had some provision for disciplining members who violate the Principles of Medical Ethics. The resolution of the House of Delegates, however, urged the creation of a special committee or some special mechanism within an existing committee that would devote particular attention to public grievances against individual physicians or against the medical profession generally. Such a committee not only would be concerned with disciplining members but would also be concerned with improving relations between the medical society and the public. During the two years that have intervened since December, 1949, most of the constituent associations have accepted this challenge. The Council on Medical Service has just completed a pamphlet on the progress that has been made in this field, and following is a brief résumé of the detailed material contained in "Medical Society Grievance Committees—A Progress Report."

At present 42 constituent associations, including the District of Columbia and Hawaii, either have created special committees or have specifically delegated this function to existing committees. Only eight associations have no program for handling grievances on a statewide basis. Of these, one has prepared a prospectus for such a committee, which is to be voted on in 1952, and three are studying the problem. Of the remaining four states, two have left the function in the hands of local societies; one has decided to postpone formation of such a committee, and one has not submitted definite information.

The following associations have committees that have as their primary function the hearing of public grievances:

Arizona	Kentucky	Rhode Island
Arkansas	Maryland	South Dakota
California	Massachusetts	Tennessee
Colorado	Michigan	Texas
Connecticut	Montana	Utah
Delaware	Nebraska	Vermont
District of Columbia	New Hampshire	Virginia
Florida	New Jersey	Washington
Idaho	New Mexico	West Virginia
Illinois	North Carolina	Wisconsin
Indiana	Ohio	Wyoming
Iowa	Oklahoma	Territory of Hawaii

The states in which this function is handled by the council of the state medical association are Georgia, Kansas, Louisiana, Minnesota, Missouri, and Nevada; the states where committees are under consideration are New York, North Dakota, Oregon, and South Carolina; and the states without committees are Alabama, Maine, Mississippi, and Pennsylvania.

COMMITTEE TITLE

Although there is considerable controversy concerning the propriety of the term "grievance committee," it remains the most popular title and is used by 19 constituent associations. Of the 15 different titles currently used, the term "mediation committee," (as used in Michigan and Montana) seems to describe most adequately the function of such a committee and at the same time is short enough to be practical. A number of state associations are considering changing the titles of their committees so as to avoid the word "grievance" and yet convey proper meaning to the public.

COMMITTEE ORGANIZATION

The effectiveness of any committee dealing with the delicate problems involved in settling complaints and grievances must necessarily depend to a great extent upon the personnel make-up of the committee. How many members should there be? How long should the members serve? How should they be elected?

Number of Members.—The sizes of the committees range from 3 to 15 members. Small committees of nine or less mem-

bers are in the majority, with the most popular being a committee of five members.

Length of Service.—Tenure of office ranges from one year to "permanent." Most of the committees, however, limit tenure to five years or less, with one year and five years being the most popular.

Selection of Members.—Committees are (1) appointed by the president, (2) composed of immediate past presidents, (3) elected by the House of Delegates, (4) or appointed by the council.

Selection of Chairman.—In most of the committees, either the members elect their own chairman or the state president makes the appointment.

MEETINGS, JURISDICTION, AND PROCEDURE

Meetings.—The great majority of the committees do not hold regular sessions but meet on call, whenever the need arises. There are some exceptions, however; for example, the Boards of Supervisors of Colorado and Utah, both of which serve as the grievance committees, meet at regular monthly intervals.

Jurisdiction.—Grievance committees are usually authorized to hear and investigate complaints concerning the professional conduct and ethical deportment of individual physicians and to attempt amicable adjustment. For the most part, their authority is limited to arbitration and does not include authority to discipline any physician. When disciplinary actions seem necessary, all evidence is usually submitted to the council or proper judicial authority. In a number of instances, however, the committee may not only refer the case to the proper judicial body but may also prefer charges and prosecute as well. In at least one state the decision of the committee is final and is so understood by both parties before a hearing is scheduled.

A few states limit the jurisdiction of their grievance committees to cases referred to them by the county medical societies, thereby acting as a sort of court of appeals; however, even in these states the committee may have original jurisdiction in cases of alleged grievances originating in areas where there are no county societies or where a county grievance committee is not functioning.

Methods of Receiving Complaints.—A majority of the grievance committees hear complaints from any source—physicians, organizations, or the general public—although a few prefer that county societies review all cases first; however, in most states complaints may be made direct to the state committee as well as through a local group. All committees accept written complaints. Only a few will accept verbal complaints. Several committees are authorized to initiate investigation when they feel it is justified, regardless of whether a complaint has been filed.

Reports and Records.—Records of hearings are kept by almost all of the committees, and all make reports on their activities to the state council or House of Delegates or both. The records of committee hearings and meetings range from complete transcripts to simple listings of the number of cases handled and settled.

Relationship with Component Societies.—Most of the committees report that they will investigate and arbitrate grievances for the local societies if so requested; however, the majority of the state associations are encouraging the component societies to establish such committees, and several are assisting in the development of local committees.

COMMITTEE PUBLICITY

About half of the reporting state grievance committees stated that the committee and its functions had been publicized. The extent of such publicity was limited in many instances to an announcement at the time the committee was established. Others continue to publicize the existence of the committee as well as the results of the committee's activities. A few committees expressed the opinion that publicity would encourage ill-founded and nuisance complaints or might be looked upon as a defensive action on the part of the association. Some associations are still considering announcing the service generally, although it appears that a number of them would prefer to handle publicity through the local societies and thus, to some extent, screen the complaints received.

Opinion on the advisability of publicizing grievance committees varies from state to state. Some medical association officers believe publicity would result in a deluge of "crank" complaints. This view has proved to be only partially correct, according to reports from committees that have been in operation several years. The consensus seems to be that this type of complaint is common during the first few months of operation, but, after a committee has been active for some time, the number of such complaints usually tapers off.

Other association officers, however, point out that the ethical physician has nothing to fear and that the quickest way to halt criticism is to face it squarely and openly. According to them, the existence of a grievance committee is not in itself sufficient to correct and eliminate existing abuses. It must be active if it is to be the means of ending malicious rumor and gossip that may bring harm to the individual physician and to the medical profession as a whole.

Where a person has actually been the victim of unprofessional or unethical conduct, the bringing of such complaints before the grievance committee affords the profession an opportunity to take action against the small minority who break faith and thereby reflect on the profession as a whole. On the other hand, when a physician has been unjustly criticized or condemned, it is to the benefit of the physician and the entire profession to clear the record of the individual physician. The grievance committee is a protective mechanism for both the public and the medical profession.

MEDICAL MOTION PICTURES

The Inner Ear (A Cinematographic Study on Some Aspects of Its Anatomy, Physiology, and Pathology): 16 mm., color, sound, showing time 35 minutes. Prepared in 1951 by H. G. Kobrak, M.D., Chicago. Procurable on loan or purchase from Doho Chemical Corporation, 100 Varick St., New York 13, and on loan from Medical Film Guild, 167 West 57th Street, New York 19.

Using a dental drill and a dissecting microscope, various parts of the inner ear are exposed on animals and human cadavers. In order to visualize the structures of the inner ear it is necessary to develop four distinct methods: (1) optical enlargement to overcome the smallness of the structures, (2) time magnification to overcome the rapidity of the phenomena, (3) artificial transparency of thin membranes in order to see the contents of the membranous labyrinth, and (4) installation of small particles in order to see hydrodynamic phenomena in the cochlea.

By combining these four methods, it is possible to expose and to photograph the mammal utricle and saccule in their full size, as three dimensional structures. The semicircular canals of fish are demonstrated, and the contents of the ampulla are made visible by the artificial transparency of the wall. It is demonstrated that the cupola extends through the whole lumen of the ampulla, which corroborates the previous claims of Steinhausen and Dohman. The acoustic function of the inner ear is shown by observation of the cochlea through windows in the otic capsule. Acoustic vibrations of the stapes footplate, the basilar membrane, and the adjacent intralabyrinthine fluids are shown through windows at various places in the otic capsule. It can be demonstrated that tones of different pitch give different vibratory patterns in the cochlea, but a full understanding of the cochlear dynamics cannot be demonstrated as yet. Ménière's disease is demonstrated by its symptomatology and histological findings. The acoustic reflex of the muscles of the middle ear is demonstrated at length. Experimental demonstrations are given which show that the most likely function of the intratympanic muscle is the protection of the inner ear against strong acoustic stimulation.

The film shows a lag between the sound and the counteraction of the tensor tympani muscle, which shows that this muscle is not in a position to protect the ear against explosions and sudden sounds; this point might have been elaborated upon in the narration. There are views of the semicircular canals from several angles, and these sequences could be edited appreciably without

detracting from the picture. The description of Ménière's disease is incomplete. It would be better to leave this section out altogether and concentrate on physiology.

In general, this is an excellent presentation. It represents an outstanding achievement in the progress of medical photography, and the author should be congratulated for this valuable contribution. It is recommended for medical students in connection with their study of anatomy and physiology of the ear and will also be of interest to otologists, audiologists, acoustic physicists, physiologists, and experimental psychologists who are interested in problems of hearing.

Glaucoma: What the General Practitioner Should Know: 16 mm., color, sound, showing time 22 minutes. Produced in 1951 by Surgis-Grant Productions, New York. Procurable on loan or purchase from Committee on Glaucoma, National Society for the Prevention of Blindness, 1790 Broadway, New York 19.

This film has been made to bring home to the general practitioner the high incidence of blindness due to glaucoma so that he will be on the watch for signs and symptoms of its existence in his patients, to show him how to recognize these signs and symptoms, and to point out the necessity of referring such patients to an ophthalmologist for a definitive diagnosis and treatment immediately. After a discussion of statistical facts about glaucoma there is a description of two cases: one, a man with acute glaucoma, and the other, a woman with chronic glaucoma. The patient with chronic glaucoma visits the general practitioner and is referred by him to the ophthalmologist. Early in the film there is a discussion of the formation and drainage of the aqueous, the maintenance of intraocular pressure, and the effects of increased pressure. The difference between congestive glaucoma, which may be either acute or chronic, and chronic simple or noncongestive is explained.

The effect of increased pressure on various parts of the eye is shown diagrammatically. The technique of tonometry done by the general practitioner using the standardized Schiøtz tonometer is briefly shown, as well as a simple test for field of vision using a white test object. The general practitioner also uses the ophthalmoscope. Unfortunately, a picture of what he observes is not shown. The ophthalmologist is shown examining the patient, using slit-lamp, gonioscope, perimeter, and tangent-screen. The dark-room and water-drinking tests are discussed as examples of useful tests for the ophthalmologist. Treatment is discussed briefly, with mention of miotics, such as pilocarpine and eserine and with diagrams showing certain types of remedial surgery, such as basal iridectomy, cyclodialysis, sclerectomy, iridencleisis, and cyclodiathermy. The film ends with the ophthalmologist thanking the general practitioner for the referral and emphasizing the need for continued supervision in order to control glaucoma. The photography, animation, and narration are well done. The film is recommended for general practitioners.

Radical Groin Dissection Malignant Melanoma: 16 mm., color, silent, showing time 17 minutes. Prepared by Jack M. Farris, M.D., Los Angeles. Sponsored by the Moore White Foundation, Los Angeles. Produced in 1951 by and procurable on rental or purchase from Billy Burke Productions, 7416 Beverly Blvd., Hollywood 36.

This film demonstrates a radical removal of a previously biopsied malignant melanoma site. It would have been helpful and would not have broken the continuity of the procedure if the formation of the flap of this phase of the procedure had been shown. The film continues by showing a radical groin dissection of the lymphatic elements. This is accomplished through an incision, which extends from the femoral triangle upward into the abdomen and parallel with the inguinal ligament. The vascular contents of the femoral triangle are dissected and exposed, and the lymph glands are removed. The abdominal dissection is accomplished by cutting through both the roof and floor of the inguinal canal. The iliac vessels are demonstrated, and the glandular elements are dissected and removed. It would have been well to either show a photomicrograph of one of the lymph glands removed or to state the microscopic findings. The photography is excellent. The technique is good, and this film can be recommended for surgeons, residents, and medical students.

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Arch. Pathology, Chicago

52:403-488 (Nov.) 1951

- *Infarction of Brain Without Thrombosis: Analysis of 100 Cases with Autopsy. S. P. Hicks and S. Warren.—p. 403.
- Studies on "Alkaline" Phosphatase Associated with Regenerating Connective Tissue Fibers. B. S. Gould and N. I. Gold.—p. 413.
- Hepatic Necrosis Induced by Dietary Means: III. Effect of Various Dietary Modifications on Liver Lipid Fractions and on Development of Necrosis. M. R. Abell and J. M. R. Beveridge.—p. 423.
- Id.: IV. Conditions Affecting Production and Prevention of Massive Liver Necrosis. M. R. Abell and J. M. R. Beveridge.—p. 428.
- Dynamics of Inflammation and of Repair: II. Chemotactic Substances in Normal Tissues. V. H. Moon and G. A. Tershakovec.—p. 441.
- Effect of Various Pathological Conditions on Copper Content of Human Tissues. E. Pedrero Jr. and F. L. Kozelka.—p. 447.
- Effect of Copper on Hepatic Tumors Produced by 3'-Methyl-4-Dimethylaminoazobenzene. E. Pedrero Jr. and F. L. Kozelka.—p. 455.
- Histochemical Analysis of Pathological Mineral Deposits at Various Sites, with Discussion of Methods Used. H. Bunting.—p. 458.
- *Single Coronary Artery: Report of Two Cases. L. A. Stapley and J. E. Edwards.—p. 470.
- Pulmonary Adenomatosis: Report of Case Demonstrating Peculiar Histological Changes in Certain Bronchioles. W. Geps.—p. 473.
- Anomalous Cardiac Blood Vessel Communicating with Right Ventricle: Observations in Case of Pulmonary Atresia with Intact Ventricular Septum. R. R. Williams, G. B. Kent Jr. and J. E. Edwards.—p. 480.

Brain Infarction Without Thrombosis.—At necropsy in 60 of 100 cases of fatal cerebral infarction, no mechanical occlusion of cerebral vessels by thrombosis, embolism, or arteriosclerosis was found, so that some other explanation for the infarction was required. The brain vessels were examined for evidence of other factors that were possibly responsible, such as cerebral arterial spasm, systemic circulatory failure, severe arteriosclerosis, and vascular hypertension. The findings were compared with those in a previously reported series of 118 cases of the hemorrhagic type of apoplexy. A common feature of hemorrhagic or infarctive apoplexy (except that caused by aneurysm) is localized cerebral ischemia. In most nonthrombotic cases the ischemia results from intrinsic focal reduction of blood flow that pathologically and clinically is best attributed to spasm of arteries and arterioles, not necessarily to the point of complete occlusion. In only a few cases could systemic circulatory failure associated with severe cerebral arteriosclerosis be implicated as a primary cause of the stroke. Probably little vasoconstriction is necessary to produce the ischemia, for interstitial edema was an outstanding gross and microscopic characteristic of the apoplectic lesions. Cerebral edema as a complication of apoplexy is discussed, and it is suggested that sodium retention in heart failure and the hypertensive state often is an aggravating factor. It is concluded that apoplexy is an ischemic disease of the brain directly caused most often by cerebral vasospasm, less often by thrombosis, and least often by systemic circulatory failure, embolism, or arteriosclerosis.

Single Coronary Artery.—A single coronary artery was revealed by necropsy in a 77-year-old man who died of carcinoma of the esophagus and in a 44-year-old woman who died of widespread malignant lymphoma. There are two main groups of single coronary arteries in adults. In one group the vessel follows the distribution of a single artery to supply the entire myo-

cardium, and the first case was an example of this type. In the other group a single vessel originates from a single ostium and immediately branches into arteries that soon follow the distribution pattern of the right and left coronary arteries, a type represented by the second case. Explanation of this anomaly by absence or ectopia of the anlage of a coronary artery is possible, although definite conclusions cannot be drawn from study of fully developed hearts.

American Journal of Medicine, New York

11:535-664 (Nov.) 1951. Partial Index

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- Account of Bilious Remitting Fever, as It Appeared in Philadelphia, in Summer and Autumn of Year 1780. B. Rush.—p. 546.
- Observations on Duties of Physician, and Methods of Improving Medicine. Accommodated to Present State of Society and Manners in the United States. B. Rush.—p. 551.
- Long Follow-Up: A Compensation of the Aging Physician. O. H. P. Pepper.—p. 572.
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- Place of Psychiatry in Medicine. E. D. Bond.—p. 588.
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- Periarthritis Nodosa: Report of Case Treated with ACTH and Cortisone. W. L. Mundy, W. G. Walker Jr., H. A. Bickerman and G. J. Beck.—p. 630.
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- Infarction of Stomach: Report of Three Cases of Total Gastric Infarction and One Case of Partial Infarction. E. B. Cohen.—p. 645.
- Ball Thrombus of Right Auricle. R. S. Radding.—p. 653.
- Disseminated Visceral Torulosis Without Nervous System Involvement: With Clinical Appearance of Granulocytic Leukemia. S. Zelman, R. H. O'Neil and A. Plaut.—p. 658.

Endocrinology, Springfield, Ill.

49:565-676 (Nov.) 1951. Partial Index

- Effects of Hypophysectomy, Growth Hormone, Thyroxine and Food Intake on Catepsin Activity of Rat Tissues. J. C. Mathies, L. Palm and O. H. Gaebler.—p. 571.
- Effect of Stress upon Ketosteroid and Non-Carboxyl Lipoid Content of Adrenal Cortex of Rat. N. Rabinovici.—p. 579.
- Comparison of Water and Saline Hydration on Diuretic Action of Sympathomimetic Agents. V. A. Drill and W. R. Bristol.—p. 589.
- Effects of Cortisone in Vivo on Oxidative Metabolism of Rat Adrenal. T. L. Sourkes and P. Henegauz.—p. 601.
- Fluid and Electrolyte Shifts in Hydrated Adrenalectomized Rat. R. C. Frost and R. V. Talmage.—p. 606.
- *Hyperplasia and I^{131} Uptake of Guinea Pig Thyroid During and After Chronic Propylthiouracil Treatment. S. A. D'Angelo, K. E. Paschkis, A. Cantarow and others.—p. 624.
- Production of Diabetes and Increased Erythrocyte Sedimentation Rate by Purified Growth Hormone. J. Campbell, H. P. Lei and I. W. F. Davidson.—p. 635.
- Effect of Growth Hormone on Muscle and Skin Collagen in Neonatal Thyroidectomized Rats. R. O. Scow.—p. 641.
- Significance of Gomori Staining of Basophils of Rat Pituitary. H. D. Purves and W. E. Griesbach.—p. 652.
- *Effect of Epinephrine and Insulin on Plasma Potassium Level. A. Dury.—p. 663.

Thyroid Hyperplasia and Uptake of Radioactive Iodine.—Immature female guinea pigs (250 to 300 gm. body weight) were given propylthiouracil for from 2 to 160 days. It was found that chronic administration of propylthiouracil induced marked hyperplastic changes in the thyroid gland, with weight increased nine to ten times after 100 to 160 days of uninterrupted treatment. The uptake of radioactive iodine (I^{131}) by the thyroid (per milligram of wet tissue) was decreased appreciably in animals receiving the propylthiouracil. The degree of depression was as great with short (2 days) as with long periods (160 days) of treatment and occurred before any anatomic changes were visible in the gland. Total radioactivity in the thyroid eventually exceeded normal when there was enough tissue to offset decreased uptake. Uptake of radioactive iodine became greater than nor-

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Titles marked with an asterisk (*) are abstracted.

mal on withdrawal of propylthiouracil. The rebound in uptake was increased in proportion to the duration of previous treatment and paralleled the course of the hyperplasia. Increased avidity of thyroid tissue for radioiodine was demonstrable, however, before anatomic change was evident in the gland. The augmented efficiency and increase in tissue mass resulted in thyroid collections of radioiodine 10 to 20 times greater than normal. Withdrawal of the goitrogen arrested the thyroid hyperplasia and resulted in considerable deposition of colloid. The observations suggest that the increased avidity of thyroid tissue for I^{131} after withdrawal of the goitrogen cannot be accounted for entirely by anatomic changes, but may reflect a change in cellular mechanism, presumably enzymatic, in response to prolonged stimulation with endogenous thyrotropic hormone.

Florida Medical Association Journal, Jacksonville
38:383-450 (Dec.) 1951

*Strokes: Their Diagnosis and Treatment. R. E. Strain and I. Perlmutter.—p. 401.
Cancer of Prostate. J. Q. Perry and A. J. Butt.—p. 406.
Disabling Conditions of Cervical Spine. F. H. Albee Jr., E. L. Jewett and E. J. Powers.—p. 410.
Fat Embolism: Report of Fatal Case. M. M. Sayet and E. W. Cullipher.—p. 416.
Intra-Abdominal Lymphangioma. R. R. Killinger, S. S. Lombardo and D. B. McRae.—p. 418.

Strokes: Diagnosis and Treatment.—The term "stroke" generally means that the patient has had a sudden paralysis. If blood is found in the spinal fluid, there is no hesitancy in saying the patient has had a cerebral hemorrhage. If no blood is found in the spinal fluid, a diagnosis of cerebral thrombosis is made. Strain and Perlmutter feel that the neurologist may be able to benefit patients with suspected cerebrovascular accidents if he sees them early and uses proper methods of study. Percutaneous cerebral angiography with a 35% solution of iodopyracet (diodrast®) introduced by inserting a needle through the skin into the carotid artery is a safe, simple, and quick method of studying the vascular system of the brain. It requires specialized x-ray equipment, a little skill, and split second teamwork with x-ray technicians. The authors performed this test over 100 times during the past year without serious complications. Case histories cited by the authors show that lesions like cerebral abscess, glioblastoma, tumor nodules, angiomas, or subdural hematoma were disclosed by percutaneous cerebral angiography in patients with "stroke" in whom a cerebrovascular accident was suspected. The more exact diagnosis of these patients will permit effective treatment of many. The authors feel that cerebral angiography could be used more frequently in patients with "strokes."

Iowa State Medical Society Journal, Des Moines
41:447-480 (Nov.) 1951

Use of Cortisone in Rheumatic Diseases. L. E. Ward.—p. 447.
The Traumatic Abdomen. J. P. Cogley.—p. 451.
*Cornpicker Accidents of Upper Extremity. C. O. Adams.—p. 454.
Use of Conditioned Reflex and Antabuse in Therapy of Alcoholism. W. E. Ash and J. D. Mahoney.—p. 456.
Physiology of Conjunctival Sac. A. M. Dean.—p. 459.

41:481-528 (Dec.) 1951
Carcinoma of Breast, Symptoms and Diagnosis. L. P. River, J. Silverstein and E. F. Dolehide.—p. 481.
Acute Cholecystitis in the Aged. W. O. Preece.—p. 485.
Diagnosis and Surgical Treatment of Posterior Wall Duodenal Ulcer. H. I. Down.—p. 488.
Orthoptics. H. O. Gardner.—p. 491.
From Leeches to Anti-Biotics. G. F. Lull.—p. 503.

Cornpicker Accidents of the Arm.—The power that operates the cornpicker is usually transmitted by a spinning power take-off bar. It is possible for a farmer to get his glove, sleeve, or hand caught on this spinning bar, and the entire arm may be rapidly wrapped about it. There may be multiple metacarpal fractures. There may be a fracture of the midshaft of the ulna, and the shaft of the radius. There may be fractures of the humerus as well, and if the motor is not stopped, the man may be killed. The numerous gears and chain drives of the cornpicker may cause injuries of the fingers and hand. The author briefly comments on repair of the digital nerves and tendons and amputation of fingers. There are also two sets of rollers,

one of which often becomes clogged with cornstalks, and while cleaning them out, the machine may be left running so that the power of the rollers helps the cleaning process. This is dangerous. The snapping rolls may cause multiple fractures, but oftenest a severe crushing injury results. One of the most important factors in the treatment of these crushing injuries is to combat the post-traumatic edema by keeping the arm high until the acute edema is under control. The treatment of the fractures usually can be combined with elevation of the extremity. Injuries sustained when the arm becomes entangled in the husking rolls of a cornpicker are even more serious. The clearance between these rolls is narrow, and any part that enters between them is usually damaged beyond repair. The victim is often able to jerk the hand out, usually with avulsion of the damaged portion. Amputations of the hand or arm are sometimes mandatory, but if there is question regarding amputation, delay with elevation of the extremity and supportive therapy will answer it and may save parts or extremities that might otherwise be amputated. A case history is presented to illustrate this point.

Journal of Bone and Joint Surgery, Boston
33A:825-1102 (Oct.) 1951. Partial Index

Surgical Rehabilitation of Hand and Forearm Disabled by Poliomyelitis. C. E. Irwin and D. L. Eyler.—p. 825.
Repair of Extensor-Tendon Insertions in Fingers. H. M. Nichols.—p. 836.
Arthritic Deformities of Wrist and Fingers. A. Steindler.—p. 849.
Preservation and Clinical Use of Freeze-Dried Bone. F. P. Kreuz, G. W. Hyatt, T. C. Turner and A. L. Bassett.—p. 863.
*Clinical Evaluation of Merthiolate Bone Bank and Homogenous Bone Grafts. F. C. Reynolds, D. R. Oliver and R. Ramsey.—p. 873.
Rupture of Brachial Artery Accompanying Dislocation of Elbow or Supracondylar Fracture. H. C. Spear and J. M. Janes.—p. 889.
Evaluation of Healed Colles' Fractures. J. J. Gartland Jr. and C. W. Werley.—p. 895.
Anomalous Tarsal Bone. A. B. Hirschtick.—p. 907.
The Skull in Paget's Disease. R. R. Goldenberg.—p. 911.
Osteopetrosis: Case Report, Autopsy Findings, and Pathological Interpretation. Failure of Treatment with Vitamin A. J. Cohen.—p. 923.
*Therapeutic Acceleration of Bone Age in Osteogenesis Imperfecta: Case Report. P. B. Wright, S. L. Gernstetter and R. B. Greenblatt.—p. 939.
Study of Displaced Capital Femoral Epiphyses. M. Cleveland, D. M. Bosworth, J. N. Daly and W. E. Hess.—p. 955.
Danger of Exposure to X-Rays by "Blind-Nailing" Technique. C. A. Rowe.—p. 967.
Clinical Applications of Ergography. F. A. Hellebrandt and S. J. Houtz.—p. 968.
Arthrodesis of Knee: Comparison of Compression Method with Non-Compression Method. H. D. Morris and R. S. Mosimain.—p. 982.
Rotation of Forearm: Experimental Study of Pronation and Supination. R. D. Ray, R. J. Johnson and R. M. Jameson.—p. 993.

Merthiolate Bone Bank and Homogenous Bone Grafts.—In a previous report Reynolds and associates discussed the clinical use of homogenous bone grafts from the thimerosal (merthiolate®) bone bank. On the basis of more extensive clinical experience, some of their earlier opinions have been revised. In 212 operations in which bone from the bone bank was used, 121 patients with 129 such operations were followed for one year or more. The authors believe that fixation and replacement are accomplished in a similar manner in autogenous and homogenous bone grafts, but that some of the cells of an autogenous graft are capable of survival. This could account both for the more rapid union of the autogenous graft as compared with homogenous graft and for the greater number of successes with autogenous grafts. With thimerosal-preserved bone the fixation and replacement are retarded, resulting in a higher percentage of failures (30.24% in this series). The thimerosal bone bank provides, however, a satisfactory method of preserving bone, and there has been no evidence of sensitivity to thimerosal. Many of the failures were not due to the homogenous bone grafts but to poor surgery. Others can be attributed to the injudicious use of bone grafts, and failure would probably have occurred with an autogenous graft. The authors now feel that homogenous grafts should be considered useful aids in orthopedic surgery rather than as universal substitutes for autogenous bone. Bone from the bank should be used when it is not feasible to use autogenous bone, such as: (1) when the available supply of autogenous bone does not fulfill the requirements; (2) when taking an autogenous bone graft will materially increase the hazard of the operative procedure; (3) when there is a chance that the graft will be lost because of infection; (4) during an

operation when it is decided that a bone graft would be useful and no previous plans for taking a graft have been made; and (5) where the bank bone is used as an internal splint when the condition would not justify taking an autogenous graft.

Acceleration of Bone Age in Osteogenesis Imperfecta.—When the child whose case is reported was 4 months old, roentgenograms showed an oblique fracture of the lower third of the left femur. The fracture healed rapidly. She again entered the hospital at the age of 2 years and 3 months because of a transverse, subperiosteal fracture of the lower third of the left femoral shaft. Following the second fracture, dietary therapeutic measures were instituted. During the next four years, she had five additional fractures of the long bones of the lower extremities, all from trivial or unrecognized injuries. Hormonal therapy was started following the fourth fracture, at the age of 4 years and 9 months, and was continued for 10 months. The medication consisted of 0.1 mg. of diethylstilbestrol daily and 10 mg. of methyltestosterone on alternate days. This combination produced a puberal development of the breasts, prominence of the mons veneris, and coarse pubic and axillary hair. During a 10-month period of hormone administration no fractures were sustained. Following the estrogen-androgen therapy, no changes were shown by roentgenograms except a striking acceleration of ossification centers. About three weeks after the medication was discontinued she had a fifth fracture. The secondary sexual characteristics regressed in the 10 months following cessation of the hormone treatment. Since the stimulus has been removed and the epiphyses have not prematurely united, it is assumed that the skeletal age will be arrested until the chronological age approaches it. Aluminum acetate therapy will be continued, if it is well tolerated and if no evidence of rickets develops. Guarded activity and cautious weight-bearing will be enforced until maturity. It is hoped that at that time there will be a spontaneous arrest of the fragility of bone, since it has been noted that the tendency to fracture diminishes after puberty. Although some patients with osteogenesis imperfecta have advanced bone age, this patient did not. The case is a striking clinical example, in which the sex hormones have accelerated osseous development in a patient with no endocrine dysfunction.

Journal of International College of Surgeons, Chicago

16:543-680 (Nov.) 1951

- Cervical Ribs: Symptoms, Differential Diagnosis and Indications for Section of Insertion of Scalenus Anticus Muscle. A. W. Adson.—p. 546.
 Carcinoma of Stomach: Plea for Earlier Diagnosis and More Radical Treatment. S. F. Marshall.—p. 560.
 Tumors of Ovary: Endocrine and Other Rare Ovarian Growths. G. F. Douglas, G. C. Douglas and G. F. Douglas Jr.—p. 567.
 Surgical Treatment of Esophageal Hiatus Hernia: Study of 42 Cases. M. X. Anderson.—p. 578.
 Evaluation of Surgical Treatment of Congenital Pulmonary Stenosis. W. J. Potts.—p. 602.
 Suction Surgical Treatment of Cataract in Children: Visual Rehabilitation. O. R. Wolfe and R. M. Wolfe.—p. 608.
 Treatment of Postsurgical Menopause by Implantation of Estradiol Pellets. S. D. Soule.—p. 622.
 Carcinoma of Pancreas with Roentgen Pattern of Nontropical Sprue: Report of Case. M. O. Cantor and L. Haking.—p. 631.
 Difficult Hernias: Use of Tantalum Mesh in Repair. A. R. Koontz.—p. 637.
 Bleeding Peptic Ulcer. E. A. Connolly and R. B. Williams.—p. 644.
 Splint for Treatment of Buttonhole Rupture of Extensor Tendon at Middle Finger Joint. R. E. Van Demark.—p. 649.
 Bilateral Successive Coexistent Tubal Pregnancies. E. Spier.—p. 654.

Surgical Treatment of Congenital Pulmonary Stenosis.—Potts' choice of a surgical procedure for treatment of congenital pulmonary stenosis is as follows: If the patient has the typical tetralogy of Fallot with the aorta descending on the left, the chest is entered through the left fourth interspace and an aortic-pulmonary anastomosis is done; if the arch descends on the right, the chest is entered through the left fourth interspace and a subclavian-pulmonary anastomosis is done. Only when the patient is less than one year of age, has a right-sided aortic arch, and cannot live without surgical relief is an aortic-pulmonary anastomosis performed on the right side. In patients who have "isolated" pulmonary stenosis a left submammary approach is made, and the stenotic valve is incised with an expanding valvulotome and enlarged with a dilator introduced through the wall of the right ventricle. Of 309 patients operated

on, 270 were subjected to a shunt operation for the tetralogy of Fallot. Of these 270, 110 were between the ages of 11 days and 3 years and 25 of them died, a mortality rate of 23%; of the remaining 160 patients between the ages of 3 and 16 years, 4 died, a mortality rate of 2.5%. Of 15 patients who underwent valvulotomy for isolated pulmonary stenosis, 1 died. Of 24 patients for whom a shunt operation was impossible, exploratory procedures terminated fatally in 11, a mortality rate of 45%. The mortality rate of congenital pulmonary stenosis is high in the first two years of life, but if a child lives into its third year the chance of survival after operation is 97%. The prognosis as to the life span is indeterminable at present. The author stresses that expert induction of anesthesia by an anesthesiologist is indispensable for the surgical treatment of congenital pulmonary stenosis; anesthesia may be induced by ether, cyclopropane, and oxygen, and ether may usually be eliminated after intubation. To prevent increased oxygen consumption associated with rise of temperature, cooling during operation was practiced routinely by placing a rubber mattress filled with cold water on the operating table beneath the moderately cyanotic child. Ice water was used for the extremely cyanotic child. Death from anoxia during operation was thus almost eliminated.

Journal of Investigative Dermatology, Baltimore

17:255-302 (Nov.) 1951

- Lipophilic Yeastlike Organisms Associated with Tinea Versicolor. M. A. Gordon.—p. 267.
 Studies on Serum Lipids in Acne Vulgaris. F. Kalz, A. Janauskas and C. Fournier.—p. 273.
 Chemistry of Human Sebaceous Gland: II. Analysis of Human Sebaceous Material from Individual Orifices. K. Schmidt-Nielsen, R. R. Suskind and E. Taylor.—p. 281.
 Multiple Hairs (Flemming-Giovannini): Report of Two Cases of Pill Multigemini and Discussion of Some Other Anomalies of Pilary Complex. H. Pinkus.—p. 291.

Journal of Neurosurgery, Springfield, Ill.

8:547-684 (Nov.) 1951

- Surgical Treatment of Acoustic Tumors. P. C. Bucy.—p. 547.
 Experimental Evaluation of Cerebral Angiography. G. A. Smith, C. M. Caudill, G. E. Moore and others.—p. 556.
 Role of Small Angiomatous Malformations in Production of Intracerebral Hematomas. G. Margolis, G. L. Odom, B. Woodhall and B. M. Bloor.—p. 564.
 Spontaneous Subarachnoid Hemorrhage in Intradural Tumors of Lumbar Sac: Clinical Syndrome. E. F. Fincher.—p. 576.
 Experimental Evaluation of Certain Contrast Media Used for Cerebral Angiography: Electroencephalographic and Histopathological Correlations. B. M. Bloor, F. R. Wrenn Jr. and G. Margolis.—p. 585.
 Value of Electromyography in Neurology and Neurosurgery. W. W. Woods and P. A. Shea.—p. 595.
 Use of Gelfoam Film as Dural Substitute: Preliminary Report. W. G. Scheuerman, F. Pacheco and R. A. Groff.—p. 608.
 Serial Electroencephalography in Acute Head Injuries. R. E. Dawson, J. E. Webster and E. S. Gurdjian.—p. 613.
 Angiographic Diagnosis of Spontaneous Thrombosis of Internal and Common Carotid Arteries. H. C. Johnson and A. E. Walker.—p. 631.
 Arteriographic Demonstration of Spasm of Intracranial Arteries with Special Reference to Sacular Arterial Aneurysms. A. Ecker and P. A. Riemenschneider.—p. 660.

Absorbable Gelatin Film as a Dural Substitute.—This report is concerned with the use of absorbable gelatin (gelfoam®) film as a dural substitute. This gelatin film is supplied sterilized in a sealed envelope, 4 by 5 in. (10.2 by 12.7 cm.) in size. It is slightly thicker than "cellophane," is transparent, and can be cut to shape. When moistened, it becomes rubbery and thus molds to contours, but tears easily. If care is exercised, it can be sutured loosely to the dura. It can be resterilized in dry heat at 140 C for four hours. No special storage or handling is necessary and the cost is low. After experimental use in dogs, the film was used clinically in 24 patients. In two patients who died at six and eight days postoperatively, autopsy revealed that the film had the same rubbery consistency as when introduced. In patients with craniotomies reoperated on within 30 days, the film was found intact; between 30 and 40 days it had become fragmented, and after 90 days it was either completely absorbed or only a few small fragments remained. The gelatin film is used to provide a barrier to the mesothelial cells of the dura at the dura-arachnoid junction, because the outer ce
 arachnoid is obviously injured at operati

have shown that at least 70 days are required for the film to be absorbed, there is more than sufficient time for the cells of the arachnoid to regenerate and thus set up a natural barrier to the formation of adhesions. The authors conclude that absorbable gelatin film is an effective dural substitute and prevents adhesions. The fact that the film is absorbed in about 80 to 90 days overcomes the disadvantage of foreign materials. The ease of handling and its low cost permits wider use than fibrin film, yet the gelatin film has all the advantages of fibrin film.

Laryngoscope, St. Louis

61:1047-1134 (Nov.) 1951. Partial Index

- Acromegaly, with Special Reference to Otolaryngological Aspect. N. B. Nachlas.—p. 1096.
- *Multiple Papilloma of Larynx: Preliminary Report of Four Cases Treated with Terramycin. I. M. Bradburn.—p. 1105.
- Otitis Externa in Puerto Rico: Clinical and Bacteriological Study of 82 Cases. M. Alonso.—p. 1114.
- Pearly Tumor of Cerebellopontine Angle: Report of Case with Reversible Deafness. M. L. Lewis Jr. and D. H. Echols.—p. 1123.

Multiple Papillomas of Larynx.—It seems possible that a virus plays some part in the production of laryngeal papillomas in children. The lesions appear as grayish-pink, mulberry-like nodules projecting from the mucosa, varying in size from a few millimeters in diameter to lesions that completely fill the larynx. They may occur anywhere in the larynx, trachea, bronchi, epiglottis, or pharyngeal wall, but are most commonly found on the true cords and ventricular bands. They are benign, sessile, or pedunculated lesions with a vascular connective tissue core covered by proliferated stratified squamous epithelium. They arise from the mucous membrane and do not infiltrate below the basement membrane. In diagnosing the cause of chronic progressive hoarseness in a child, papilloma, vocal nodules, "screamers' nodes," chronic laryngitis, congenital cysts and webs, congenital laryngeal stridor, laryngotracheitis, hypertrophy of the ventricular bands, foreign body, paralysis of the recurrent laryngeal nerve, syphilis, and tuberculosis must be considered. There are many treatments for multiple papilloma but none of them produce consistent results. The papillomas tend to disappear at puberty. Gentle forceps removal under direct laryngoscopy is perhaps the best surgical procedure. This may be augmented by tracheotomy to obtain an adequate airway. Four cases are reported in which terramycin was given following removal by forceps. Two patients were free of papilloma after two months of treatment. Two patients were improved but still had papilloma. Terramycin given in relatively large doses after surgical removal appears to have some beneficial effects in multiple papilloma. It seems necessary to give it in a dosage of 50 mg. per kilogram of body weight per day, for not less than two months. The apparent effect of terramycin on multiple papilloma supports the theory of a virus etiology of multiple papilloma.

Medical Annals of District of Columbia, Washington

20:583-640 (Nov.) 1951

- *Management of Critical (Massive) Gastroduodenal Hemorrhage. C. S. White, E. C. Wilson Jr. and C. S. White Jr.—p. 583.
- Types of Psychotherapy. R. A. Cohen.—p. 589.
- Chronic Alcoholism. R. P. Odenwald.—p. 596.
- Idiopathic Simple Arterial Thrombosis: Report of Case. P. A. Reed.—p. 602.
- Sporotrichosis: Report of Case in Greater Metropolitan Washington. M. A. Weiner.—p. 606.

Management of Critical Gastroduodenal Hemorrhage.—White and associates suggest that "critical" should be substituted for "massive" in reference to serious hemorrhage associated with gastric and duodenal ulcers. In trying to define critical hemorrhage, the authors state that, although it is impossible to measure the blood lost, it is possible to measure the quantity and quality of the blood remaining in the vascular system. Although no hard and fast rule can be applied, it has been proposed that if the red blood cell count is 2,500,000 or less or the hemoglobin level 7 gm. or less per 100 cc., or, if 2,500 cc. of transfused blood is required to restore the patient's blood to its normal volume and cellular content, it can be stated that the patient has had a critical hemorrhage. A more accurate index can be obtained by estimating the blood volume by the Evans' method. The authors show that it is impossible to differentiate exactly

those that may be expected to recover with medical treatment only and those who should be treated surgically. They stress the following points: 1. Multiple transfusions are mandatory and arterial transfusions may be necessary. 2. Patients over 45 years of age have a higher mortality with critical hemorrhage than those below that age, but factors other than hemorrhage contribute to the mortality. 3. If repeated transfusions are not followed by cessation of bleeding, as determined by blood pressure and blood examination, operation is indicated. 4. Shock is not a contraindication to operation if ample blood for transfusion is available. 5. Gastric resection is the operation of choice for the gross ulcer. 6. Ligation may suffice in the small necrotic type of ulcer.

Military Surgeon, Washington, D. C.

109:683-756 (Dec.) 1951. Partial Index

- Practice of Field Medicine on Operation "Killer." J. F. Harris.—p. 683.
- Battle Wounds of Colon and Rectum. B. P. Colcock.—p. 688.
- Medical Support for Mountain Fighting in Korea. P. T. Buerger.—p. 694.
- Eye Conditions Similar to Those Produced by Modern Warfare. R. I. Pritkin and M. L. Duchon.—p. 706.
- Dynamic Group Experience in Military Hospital Paraplegic Unit. R. J. Margolin and C. L. Rose.—p. 712.
- Duodenal Ulcer: Pathogenetics, and Re-Evaluation of Therapeutics. R. de R. Barondes.—p. 720.

Missouri State Medical Assn. Journal, St. Louis

48:845-940 (Nov.) 1951

- Congenital Malformations Remedial During Early Infancy. J. A. Bigler.—p. 861.
 - Oral Cholecystography: Experiences with Newer Cholecystopaques. W. G. Scott and W. A. Simril.—p. 866.
 - Roentgen Therapy in Bursitis of Shoulder: Analysis of 50 Cases Using Both Deep and Superficial Techniques. C. M. Witt and P. F. Titterington.—p. 870.
 - Strangulated Femoral Hernia: Review of 108 Cases. J. C. Peden Jr.—p. 873.
 - *Study of Sympathetic Blocks: Consideration of Factors Affecting Clinical Results. B. W. Harned and F. V. Theis.—p. 882.
- 48:941-1020 (Dec.) 1951
- The Spinal Puncture. D. F. Coburn.—p. 957.
 - Eye Care in Battalion Aid Stations. E. B. Alvis.—p. 958.
 - Surgical Treatment of Achalasia. W. A. Bowersox and R. S. Kieffer.—p. 960.
 - New Agent for Treatment of Migraine and Histaminic Cephalalgia. R. B. Ryan.—p. 963.
 - The Physician and Oral Health in Children. J. A. Bigler.—p. 966.

Results of Sympathetic Blocks.—Interpretation of the results of sympathetic block is uncertain since it is not possible to differentiate organic occlusion of the vessels and failure of the block. Harned and Theis describe investigations of the effect of proved sympathetic blocks in patients whose symptoms might be benefited by temporary sympathetic nerve block or those who were considered for sympathetic neurectomy. Oscillometric readings were taken on the ankle, leg, and thigh; peripheral skin temperature was determined at selected sites on the foot, toes, and leg; and skin resistance determinations were repeated three times before the nerve block to assure stabilization of these determinations. After the sympathetic nerve block the oscillometric and skin temperature readings were repeated. Then, the patient was warmed by being covered with blankets and an electric pad, and the skin resistance studies were repeated. The resistance studies were made with the neurodermometer, a specially constructed ohmmeter. The elimination of sweat gland activity resulting from the block greatly increases the skin resistance to passage of minute electric currents as compared to the normally innervated areas. Skin temperature determinations are valuable in studies of this type; however, the temperature of initially warm extremities cannot be further elevated by sympathetic block, although the accompanying pain may be relieved. Oscillometric readings are rarely changed materially by sympathetic blocks, because sympathetic activity is mainly to small arterioles and capillaries, and oscillometric readings determine the tonicity of the larger arterioles and arteries. Therefore, the neurometer is the simplest and most reliable means of demonstrating the success of sympathetic blocks. The best clinical results following sympathetic blocks are in relieving pain and vascular spasm of recent origin, but blocks should be tried on even seemingly "hopeless" obliterative vascular disease.

Nebraska State Medical Journal, Lincoln

36:345-376 (Nov.) 1951

- Lung Tumors as Pathologist Sees Them. W. A. Meissner.—p. 347.
 Use and Abuse of Bronchography in Lung Disease. M. A. Kellett.—p. 350.
 Prevention and Treatment of Eclampsia. L. D. Odell.—p. 352.
 Subdural Hematoma in Absence of Objective Neurologic Findings. L. J. Gogela.—p. 357.
 Diverticulitis May Mask Carcinoma of Colon. J. H. Brush.—p. 360.
 Primary Dysmenorrhea—Its Gynecological, Physiological and Psychiatric Aspects: Review of Literature. G. R. Pullman.—p. 363.

36:377-408 (Dec.) 1951

- Massive Gastro-Intestinal Hemorrhage. A. Sachs.—p. 379.
 Early Diagnosis of Carcinoma of Cervix. L. S. McGoogan.—p. 382.
 Myelography and Intervertebral Disc Lesions of Low Back. F. S. Webster.—p. 386.
 New Concept in Management of Idiopathic Pruritus Ani: Preliminary Report. G. R. Underwood.—p. 391.
 Educational Plan of American Academy of General Practice. T. D. Fitzgerald.—p. 392.
 Pull-Through Operation for Ano Rectal Carcinoma. L. Anderson.—p. 394.
 Clinical Electroencephalography in Convulsive Disorders. R. J. Ellingson.—p. 396.

New England Journal of Medicine, Boston

245:711-752 (Nov. 8) 1951

- Neurocirculatory Asthenia, Anxiety and Neurosis. H. H. W. Miles and S. Cobb.—p. 711.
 Control of Inoperable Oral Cancer with Massive Roentgen Therapy. G. White and W. R. Christensen.—p. 719.
 Suicidal Dilantin (Sodium Diphenylhydantoin) Poisoning: Case Report. J. B. Tichner and C. D. Enselberg.—p. 723.
 Roentgen Therapy in Acne. G. M. Crawford, R. H. Luikart Jr. and R. F. Tilley.—p. 726.
 Cerebral Palsy. E. Denhoff, V. N. Smirnoff and R. H. Holden.—p. 728.

245:753-792 (Nov. 15) 1951

- Coronary Arteriosclerosis and Myocardial Hypertrophy. E. P. Connolly and D. Littmann.—p. 753.
 Effect of ACTH in Trichinosis: Clinical and Experimental Study. M. A. Luongo, D. H. Reid and W. W. Weiss.—p. 757.
 Fatal Transfusion Reactions from Massive Bacterial Contamination of Blood. C. W. Borden and W. H. Hall.—p. 760.
 Diabetic Coma Versus Diabetic Nephropathy: Hazards of Factitious Insulin Resistance, Oliguria and Hyperkalemia. H. F. Root, R. D. Story and J. B. Cortesi.—p. 765.
 Cerebral Palsy. E. Denhoff, V. N. Smirnoff and R. H. Holden.—p. 770.

Roentgen Therapy in Acne.—Results are reported for 58 patients with acne, 5 to 20 years after roentgen therapy. The acne was papulopustular in 36 patients, deeply indurated or nodular in 14, and cystic in 8. The degree of activity was moderate in 30 cases and severe in 28; the average duration had been 5.6 years. The average age of the patients at the time of roentgen therapy was 21.4, the youngest being 15 and the oldest 38. The face was treated with two exposures, each side receiving from 60 to 75 r; an additional central face dose of 15 r was given to some patients. Voltage varied from 75 to 100 kv., and unfiltered radiation was generally used. The maximum number of roentgens administered varied from 500 to 1,450. Immediate results were excellent in 35 patients, unsatisfactory in 4, and partially successful with occasional lesions observed in 19 patients. In the follow-up telangiectasia was found in nine patients, 30 to 41 years of age, five of whom had received less than 800 r. It was relatively inconspicuous and was probably due to causes other than roentgen therapy. Any group of persons between 30 and 40 years of age may show a similar incidence of telangiectasia without previous roentgen radiation. None of the patients showed atrophy, pigmentary changes, or keratoses. Best results and fewest recurrences were observed in patients who had received 1,000 to 1,200 r in an uninterrupted series of treatments.

Pennsylvania Medical Journal, Harrisburg

54:1017-1112 (Nov.) 1951

- Hormone Therapy of Cancer. D. C. Hines.—p. 1045.
 Cutaneous Diseases Associated with Diabetes. W. B. Guy.—p. 1052.
 Valoctin Therapy in Functional Dysmenorrhea: Preliminary Report. L. Z. Goldstein.—p. 1056.
 Management of Diarrhea in Infancy. J. P. Scott.—p. 1058.
 Effect of ACTH and Cortisone on Skin and on Skin Diseases. H. Blank.—p. 1052.

Postgraduate Medicine, Minneapolis

10:359-458 (Nov.) 1951

- *Nonoperative Treatment of Perforated Duodenal Ulcer. S. F. Seeley.—p. 359.
 Post-Coronary Syndrome. N. Flaxman.—p. 367.
 Biliary Tract Calculi and Associated Disease. L. T. Palumbo.—p. 370.
 New Type of Plaster Apparatus for Continuous Traction and Immobilization of Cervical Spine. J. P. Chaves.—p. 377.
 Treatment of Intracranial Aneurysms. J. L. Poppen.—p. 380.

Nonoperative Treatment of Perforated Duodenal Ulcer.—Seeley reviews 106 cases of perforated duodenal ulcer treated without operation. One death occurred in a patient who was being treated for a myocardial infarction with cardiac failure. The mortality rate of 0.9% (one death in 106 cases) is compared with the mortality rates in several series of cases in which surgical treatment was used. Although a mortality as low as 1.1% was reported in 1946 in 88 cases with surgical treatment, as late as 1948 a mortality of 18% was reported in 101 cases, and in a series of 15,340 cases between 1930 and 1940, the mortality was 23.4%. With nonoperative treatment immediately on admission of a patient with suspected perforation of a peptic ulcer, a Levin tube is passed, the gastric contents are aspirated, and 1.4 grain of morphine sulfate is given intramuscularly. Constant decompression of the stomach is the most important feature of the treatment. During the first 24 hours 3,000 cc. of fluid is administered intravenously, including at least 1,000 cc. of 5% glucose in isotonic sodium chloride solution and 1,000 cc. of sixth-molar sodium lactate injection. The remaining 1,000 cc. of solution was usually 5% glucose in water. The amounts of intravenously administered fluids are changed in accordance with the urinary output, the aim being to insure an average daily output of 1,500 cc. In many cases thiamine chloride, nicotinamide, riboflavin, menadione (vitamin K), liver extract, and ascorbic acid were added to the intravenous solutions. In the presence of hypoproteinemia or anemia, whole blood was given. Antibiotics and chemotherapeutic agents were given in a preparation of 1,000,000 units of penicillin, 1 gm. of streptomycin, and 2.5 gm. of sodium sulfadiazine in 1,000 cc. of isotonic sodium chloride solution or 5% glucose in water. This is given over a 12 hour period by slow intravenous drip and repeated every 12 hours until about the fifth day. Since this solution accounts for only 2,000 cc. of intravenous fluid daily, one of the solutions referred to under intravenous therapy is added to increase the total fluid intake. By the 14th day, if no complications have developed, patients are transferred to the medical service. Complications occurred in 16 of the 106 cases of perforated duodenal ulcer treated by nonsurgical means. Abscesses developed in eight patients (four subphrenic, two upper abdominal, and two pelvic). Other complications were pleural effusion in four cases, drug psychosis in two, and pneumonitis and thrombophlebitis in one case each. Seven patients were subsequently operated on for chronic duodenal ulcer, but no fluid or foreign material was found in the peritoneal cavity. Adhesions were no more numerous than when surgical closure had been done.

South Carolina Medical Assn. Journal, Florence

47:435-472 (Dec.) 1951

- Antepartum Bleeding in Last Trimester. H. H. Fouche.—p. 435.
 Medical Aspects of Control of Rabies. B. F. Wyman.—p. 438.
 Hospital Facilities for Premature Infant in South Carolina. J. I. Waring.—p. 441.
 "What Do You Get for Your \$25?" W. W. Bauer.—p. 443.
 Brighter Outlook for America's Cerebral Palsied. C. F. McKhann.—p. 446.
 Epidermoid Carcinoma of Cervix: Statistical Study. J. L. Simpson, L. L. Hester and J. M. Wilson.—p. 448.

West Virginia Medical Journal,

47:347-376 (Nov.) 1

- Diagnosis and Treatment of Diabetic Surgical Complications of Diabetes
 Indications for Hysterectomy. J. L. Traumatic Lesions of Urinary
 D. R. Gilbert and A. I.

FOREIGN

Annals of Rheumatic Diseases, London

10:217-392 (Sept.) 1951

- Anti-Rheumatic Activity of Several Steroids. R. Liefmann.—p. 233.
- Amyloidosis in Still's Disease. J. A. James and F. G. Bolton.—p. 250.
- Response of Schoenlein-Henoch Syndrome to ACTH: Report of Case with Serial Skin Biopsies. J. E. Levinson, M. Horwitz, J. P. Kulka and others.—p. 255.
- Differential Tissue and Organ Anoxia in Disease: Measurement of Pericardial Oxygen Saturation Levels in Patients with Arthritis. J. W. L. Doust.—p. 269.
- Punch Biopsy of Synovial Membrane. H. F. Polley and W. H. Bickel.—p. 277.
- Sjögren's Disease and Rheumatoid Arthritis. S. R. Reader, H. M. Whyte and P. C. Elmes.—p. 288.
- Spontaneous Rupture of Tendon of Extensor Pollicis Longus as Complication of Rheumatoid Arthritis. R. Harris.—p. 298.
- *Monarticular Trauma and Rheumatoid Arthritis. M. Kelly.—p. 307.
- Splenectomy in Rheumatoid Arthritis. R. Bach and J. H. Jacobs.—p. 320.
- Copper Treatment of Experimental and Clinical Arthritis. W. C. Kuzell, R. W. Schaffarick, E. A. Mankle and G. M. Gardner.—p. 328.
- Rheumatoid Nodules: Study in Their Pathogenesis and Effects of Cortisone and ACTH. T. E. Hunt and A. J. Blanchard.—p. 337.
- Knee Effusion in Young Adults as Early Sign of Degenerative Arthritis. R. W. Parnell.—p. 347.
- Gout: Observations on Effects of Drugs on Plasma Uric Acid and Urinary Uric Acid. G. D. Kersley, L. Mandel and E. Bene.—p. 353.
- Comparative Therapeutic Value of Massage with "Adrenaline Cream" and with Another Cream in Conditions Associated with Deep Pain. E. G. L. Bywaters.—p. 359.

Monarticular Trauma and Rheumatoid Arthritis.—Local trauma may result in chronic monarticular arthritis, but there are also reports that indicate that monarticular trauma may induce rheumatoid arthritis. Kelly's experience confirms that injury may produce chronic polyarthritis. In more than 50 patients of 600 observed, injury was the sole visible factor; but this study is confined to 32 patients in whom the first symptoms appeared immediately after an injury to a single joint. The joint remained painful and swollen for periods varying from one week to two years before a second joint was involved, and in most cases a number of joints were then affected in a short time. The arthritis appeared first in the opposite joint in 13 cases, and simultaneously in two symmetrical joints in 12. The persistence of chronic arthritis in an injured joint depends on two factors: further damage to the joint by overstrain, and reflex disturbance of joint physiology. The spread to other joints frequently followed overstrain or further damage to the injured joint; symmetry suggests that the change is propagated through nervous channels. It is concluded that the constitutional factor that favors the spread of the disease is not a permanent defect but a late disturbance of the nervous system induced by impulses from the damaged tissues.

British Medical Journal, London

2:1295-1358 (Dec. 1) 1951

- Adrenal Cortex and Rheumatoid Arthritis. E. C. Kendall.—p. 1295.
- Influence of Unilateral Nephrectomy on Production of Experimental Arthritis in Albino Rat. R. G. Harrison.—p. 1299.
- Sympathectomy and Innervation of Kidney. Z. M. El Asfoury.—p. 1304.
- Haemoglobin Levels Before and After Labour. H. E. Magee and E. H. M. Milligan.—p. 1307.
- Diffuse Arteritis of Unknown Origin Accompanied by Eosinophilia. K. W. Walton and D. W. Ashby.—p. 1310.
- Multiple Argentaffinoma of Ileum Revealed by Secondary Growth in Epididymis. J. R. O'Brien.—p. 1315.
- Argentaffin Tumor of Ileum with Perforation. I. S. Stewart and G. R. Thomson.—p. 1316.
- Effects of Hyperthermia and Antibacterial Agents on Tubercle Bacilli. J. Marks.—p. 1318.
- Unusual Method of Treating Hydrocephaly. A. U. Campbell.—p. 1320.

Adrenal Cortex and Rheumatoid Arthritis.—Kendall reviews the history of cortisone and corticotropin, discussing the chemical phase of investigation and the physiological and pharmacological aspects of these drugs. Then he discusses rheumatoid arthritis and its possible causes and the dosage of cortisone and corticotropin. He concludes that rheumatoid arthritis and rheumatic fever, as well as other collagen diseases, are related in pathogenesis and respond in similar ways to cortisone. Perhaps the most hopeful aspect of the study is the wide clinical application of this hormone. The unexpected and far-reaching influence of cortisone on many diseases may be produced through its control of some causative agent common to all of them. The nature of

this agent is unknown, but the author agrees with Pickering and Meiklejohn that the hypothesis of the adaptation syndrome of Selye is not acceptable. Today it can be said that cortisone relieves the pain and symptoms of rheumatoid arthritis and is a life-saving measure in other syndromes, but to the clinician interested in research it will be a means of investigating many long-unresolved problems.

Irish Journal of Medical Science, Dublin

311:505-552 (Nov.) 1951

- Experimental Evaluation of Antibacterial Agents in Tuberculosis Therapy. W. H. Feldman.—p. 505.
- Technique of Eosinophil Counting. S. M. Shea.—p. 528.
- Intravenous Pethidine. M. Murphy.—p. 535.
- Action of Vibrio and Influenza Virus Enzymes and of Periodate and Trypsin on Human Red Cells. F. S. Stewart and P. N. Meenan.—p. 541.
- Ringworm Species in Eire. F. O. C. Meenan.—p. 546.
- *Pathognomonic Sign of Leakage of Cerebrospinal Fluid Into Subdural Space. A. A. McConnell.—p. 550.

Sign of Leakage of Cerebrospinal Fluid into Subdural Space.—Cerebrospinal fluid cannot be absorbed anywhere except from the subarachnoid space over the convexity of the brain. If the arachnoid membrane is torn, cerebrospinal fluid escapes into the subdural space, where it remains indefinitely. This leakage of cerebrospinal fluid is a common occurrence in cases of closed head injuries. In 212 patients operated on, it was found 101 times, while the number of patients with all types of intracranial hemorrhage was 102. It is particularly common in patients who survive but are not recovering. Of 19 of these patients who submitted to air encephalography, air was seen in the subdural space on the second day in 17, and in all these the characteristic fluid was found at operation. Pneumoencephalography is very helpful in these cases. The pictures taken immediately may reveal some abnormality of the brain, and the second-day pictures taken in the erect position may show the fluid level and that air has accumulated in the subdural space. Such an appearance is evidence of excessive amounts of fluid in the subdural space. Such fluid accumulations can produce or exaggerate various post-traumatic symptoms, such as headache, lack of concentration, impairment of memory, dizziness, irritability and the defeatist attitude so marked in some patients after a head injury. If excessive fluid is shown in the subdural space by the second-day encephalogram, it should be removed through burr-holes in the skull.

Lancet, London

2:997-1046 (Dec. 1) 1951

- The Power of Words. V. B. Carter.—p. 997.
- *Treatment of Arterial Hypertension with Veriloid (Veratrum Viride). R. Kauntze and J. Trounce.—p. 1002.
- Polymer-Fume Fever. D. K. Harris.—p. 1008.
- *Diuretic Effect of Isotonic Saline Solution Compared with That of Water: Influence of Diurnal Rhythm. G. Blomhert, J. Gerbrandy, J. A. Molhuysen and others.—p. 1011.
- Variations in Response to Relaxant Drugs. J. W. Dundee and T. C. Gray.—p. 1015.
- Myasthenia Gravis and Malignant Exophthalmos: Report of Case. H. Zondek and A. Ticho.—p. 1018.
- Haemoglobinuria in Typhoid Fever Treated with Chloramphenicol. C. E. G. Smith.—p. 1020.
- Correlation of Height and Weight in Early Childhood. H. V. Muhsam.—p. 1021.

Veratrum Viride in Treatment of Hypertension.—"Veriloid," a stable and potent mixture of ester alkaloids of veratrum viride, was given orally to seven men and seven women with hypertension for periods up to 11 months. The hypertension was of the essential type in nine patients and of the malignant type in one. In two it resulted from chronic pyelonephritis, and in two others from chronic nephritis. In all the hypertension was severe and, except in one case, it was associated with symptoms. The patients' ages ranged from 19 to 62. The results in four of the patients, one with chronic nephritis, one with chronic pyelonephritis and two with essential hypertension, have been outstanding. The patient with chronic nephritis was observed for 11 months, during which withdrawal of "veriloid" was followed by return of the blood pressure to former levels and an attack of encephalopathy. Control was re-established on resumption of

"veriloid" therapy. The other three patients of this group of four were treated for more than three months. Each of these patients was young, and the dosage was about 12 mg. daily, except in one for whom 26 mg. daily was necessary. In four other patients, one with malignant and three with essential hypertension, the treatment with "veriloid" failed. One patient with chronic pyelonephritis died of renal failure although toxic symptoms were an ever-present difficulty, hypertensive crises were averted with "veriloid." One youth of 19 with chronic nephritis and hypertensive encephalopathy died a month after discharge from a cerebral vascular accident. Although the outcome of his disease was uninfluenced by the drug, he obtained much symptomatic relief. Of the four remaining patients who had essential hypertension, three were benefited, but in the other one hypertension progressed despite treatment. The authors conclude that "veriloid" by mouth will lower the blood pressure in about two-thirds of patients with hypertension. In half of these the therapeutic level may so closely approach the toxic level as to make its daily use in nonhospitalized patients unsuitable, so that the drug is a satisfactory hypotensive agent for 20 to 30% of patients with hypertension.

Diuretic Effect of Isotonic Sodium Chloride Solution and of Water.—Blomhert and associates compared the diuretic effect of isotonic sodium chloride solution, administered orally or intravenously in a short time, with the diuretic effect of equal amounts of water. Owing to the diurnal excretory rhythm different reactions at different periods of the 24 hours could be expected, and experiments were made both by day and by night, mostly in healthy male students. In the daytime diuresis after drinking of two liters of water was complete, the average output being 2,026 ml. in four hours. During the night only 70% of this amount was excreted in the same time. The diuretic response to 2 liters of isotonic sodium chloride solution administered orally or intravenously in one hour by day was diphasic. In the first hour and a half the diuresis was like that seen after the drinking of plain water; about 750 ml. of urine with a low chloride content was excreted in two hours, and a protracted mild saline diuresis followed. During the night the response to the drinking of 2 liters of sodium chloride solution was restricted to a brief water diuresis (average 630 ml.). All the solution given intravenously was retained. These facts may help to explain the onset of cardiac asthma at night. After the intake of sodium chloride solution a temporary increase (average 350 ml. or 18%) in the volume of circulating blood plasma, as manifested by a dilution of hemoglobin and serum proteins, and an increase in central venous pressure were found. Comparison of these experimental data with clinical observations suggests that secretion of antidiuretic hormone depends not only on the osmotic pressure of the body-fluids but also on the circulation. In an addendum to this report the authors direct attention to a recent report in an American publication in which Strausz and co-workers describe the production of a "water diuresis" by intravenous injection of sodium chloride solution. This diuretic response was found only in recumbent subjects.

Medical Journal of Australia, Sydney

2:581-612 (Nov. 3) 1951

- Rheumatoid Arthritis. S. Nelson.—p. 581.
 Orthopaedic Aspects of Rheumatoid Arthritis. G. Colvin.—p. 585.
 Modern Trends in Radiotherapy. A. G. S. Cooper.—p. 588.
 Obstetric Emergencies Following Deliveries. D. F. Lawson.—p. 592.
 Ascariasis in Sydney Children and Its Relation to Urban Backyard. T. C. Backhouse and A. J. Bearup.—p. 595.
 Virus Isolated from Case Resembling Epidemic Pleurodynia: Preliminary Report. D. W. Howes.—p. 597.

2:613-656 (Nov. 10) 1951

- Histopathological Study of 11 Cases of Poliomyelitis, Including One in the Newborn. M. Fowler.—p. 613.
 Transmission of Contagious Ecthyma from Sheep to Man. V. M. Pask, I. M. Mackerras, A. K. Sutherland and G. C. Simmons.—p. 628.
 Rupture of Liver in the Newborn. F. Arden.—p. 632.

Histopathological Study of Poliomyelitis.—This study is based on an examination of material obtained from 10 of the 20 individuals who died in the 1947-1948 epidemic in South Australia. The brains of five patients and the brains, cords, and various peripheral ganglia from the remaining five patients were

examined. The olfactory bulbs were available in all cases. Many of the infections were bulbar in type and some patients died early in the disease. The author confirmed many of the pathological observations reported by earlier investigators, but in addition he stresses the following points: 1. Involvement of the basal nuclei of the pons, although moderate, is not uncommon. 2. Lesions on the periphery of the red nucleus tend to be more frequent on the medial borders. 3. Purkinje's cells are not completely spared from destructive changes. 4. Betz's cells are not the only components of the motor cortex destroyed; in some areas they were spared, although the smaller pyramidal neurons were involved. 5. All layers except layer 1 of the motor cortex were affected; layers 5 and 6 were affected most commonly. Entry of virus from the tonsillopharyngeal region in the bulbar cases was suggested by the nature of the lesions in the nucleus ambiguus. Whether motor or sensory fibers participate in the transfer of virus is equivocal, although circumstantially it is more likely that the latter are involved. The lesions in the medulla oblongata are not necessarily uniform, being modified by such factors as the route of invasion. There is some basis for the belief that virus, in the absence of symptoms of the disease, may exist in the nervous system without histological evidence. On the other hand, there is only meager evidence that in patients with paralysis neurons of known susceptibility may harbor virus in the absence of microscopic change. Lesions in peripheral ganglia cannot be considered evidence that the virus enters by way of peripheral nerves without more rigid criteria than some currently in vogue. Massive pulmonary embolism is a rare complication of poliomyelitis, but in one case might have been prevented by passive massage without joint movements. A previously unobserved form of poliomyelitis of the brain stem, thought to be poliomyelitis, is described. It was unusual because of the age of the patient, who died 13 days after birth, and because the necrotic lesions of the neurons were not associated with a mesodermal reaction.

Medicina, Buenos Aires

11:283-344 (Oct.) 1951. Partial Index

- *Ten Years of Premarital Examination. T. Padilla and A. Speroni.—p. 283.
 *Action of Ultrasound on Spleen. R. R. Santoro and G. F. Sommersguter.—p. 290.
 Clinical Value of Modifications of the QT Interval. M. Klotzman.—p. 294.
 Simplified Method for Obtaining the Thyroid Cytological Coefficient Used in Determination of Thyrotropin. E. Del Conte and J. F. E. Vasena.—p. 312.

Premarital Examination for Syphilis.—A law requiring premarital examination of men but not women for venereal disease was enacted in Argentina in 1939. Syphilitic chancre, syphilids, chancroid, transmissible gonorrhea, venereal lymphogranuloma, venereal granuloma, and papilloma are considered legal obstacles to marriage, which is not permitted until the candidate becomes non-infectious. Premarital examination was made on 5,204 men in the Hospital de Clínicas de Buenos Aires from 1940 to 1949 inclusive. The Wassermann and Kahn tests gave strongly positive results in 87 candidates. In the same decade 264,648 marriages took place in Buenos Aires. From these figures it was calculated that 5,072 individuals in Buenos Aires and 25,000 individuals in Argentina get married with positive reactions for syphilis. An inquiry among three groups of persons showed that only 47% of medical students, 49% of clerks, and 41% of workmen had knowledge of the law and understood its meaning. A total of 9,890 routine Kahn and Wassermann tests were made in the aforementioned hospital in the five years from 1945 to 1950. Positive results for syphilis were obtained in 6.14% in men and in 7.42% in women. An inquiry was made among white collar girls and among women working in factories to determine whether they wished to be included in the law requiring premarital examination for syphilis. All women in both groups answered in the affirmative. The authors suggest reform of the law to include women.

Effect of Ultrasounds on Spleen.—The spleens of four normal rabbits were exposed to ultrasonic irradiation through the shaved skin. Two additional rabbits were used as controls. The irradiations were given at a power level of 40 watts for 15 minutes

every other day up to a total of 20 applications. The irradiated animals had pronounced leukopenia, but the number and resistance of the erythrocytes were normal. The spleens of the irradiated animals were grossly of same size and form as those of the controls. Histologically, however, they showed a great increase of red pulp and diminution of white pulp, with a decrease in the number and size of the lymphatic nodules, which in certain zones had entirely disappeared. This was due to the destruction of lymphoblasts and young lymphocytes, which are very sensitive to the effects of ultrasound.

Nordisk Medicin, Stockholm

46:1513-1552 (Oct. 10) 1951. Partial Index

- Treatment of Pregnancy Toxemia: Results from St. Erik's Hospital 1942-1948. G. Nordenstrahl and L. Werkö.—p. 1519.
- *Tuberculous Salpingitis: Clinical Study of 61 Cases. G. Berggren.—p. 1522.
- Genital Tuberculosis and Pregnancy. S. Kullander.—p. 1527.
- Teratoma Operated on Immediately After Birth. A. Sjövall.—p. 1531.
- Talcum Powder Granuloma in Abdomen. B. G. Wallerström.—p. 1532.

Tuberculous Salpingitis.—Berggren's 61 cases of histologically verified tuberculous salpingitis comprise 40 cases of manifest tuberculous salpingitis and 21 cases of latent tuberculous salpingitis, the latter treated surgically for sterility. Operation was done in 38 cases of the first group; it was contraindicated in two. In operation on the tuberculous genital organs all diseased tissue was removed and as much ovarian tissue as possible was retained. Streptomycin was applied in four cases, apparently with good effect in two. Follow-up of the 54 surviving patients from 3 months to 12 years after discharge showed that in 32 of the 33 patients in the first group the genital tuberculosis had healed, but two had progressive pulmonary tuberculosis. Of the 21 in the second group, 20 had recovered without complications; the remaining patient was later treated with streptomycin and subsequently operated on, with recovery. Surgical treatment of latent tuberculous salpingitis did not affect sterility. The author believes that with streptomycin and other antibiotics and agents such as *p*-aminosalicylic acid (PAS) the treatment of tuberculous salpingitis will in the near future become more conservative.

Philippine Medical Association Journal, Manila

27:543-590 (Sept.) 1951

- Cases of Pericarditis Autopsied in College of Medicine from January, 1947, to May, 1950. A. G. Sison, L. Gomez, P. C. Campos and R. A. Apostol.—p. 543.
- Aureomycin Therapy in Acute Infectious Hepatitis with Jaundice. R. W. Kalmansohn, E. A. Cleve and F. W. Pruitt.—p. 549.
- Present Status of Immunization. Fe del Mundo.—p. 554.
- Progress of Orthopedics in Philippines. J. S. Santillan and D. J. Tablan.—p. 558.
- Concise Pharmacology of Some Drugs Used in Ocular Therapeutics. R. Guevara.—p. 563.

Presse Médicale, Paris

59:1533-1564 (Nov. 21) 1951. Partial Index

- *Present-Day Treatment of Cutaneous Tuberculosis. C. Huriez.—p. 1538.
- Modern Treatment of Chronic Purulent Pleurisy. H. Métras, M. Warnery, M. Grégoire and others.—p. 1554.

Present-Day Treatment of Cutaneous Tuberculosis.—The author observed 230 cases of cutaneous tuberculosis in the neighborhood of Lille from 1941 to 1951. Chest roentgenograms of 120 patients were studied. One-half showed no abnormalities on roentgenograms, one-fourth had lymph node involvement following thoracic disease, and one-fourth showed pleuropulmonary lesions. There were 129 women and 101 men among these patients. The influence of insufficient sunshine may be seen in the fact that 33% of the men were miners. More than half of the patients had contracted their skin lesions before the age of 20; 39% between 20 and 60 years, and only 4% after 60. Skin lesions were of the following types: lupus vulgaris, 141; verrucous, 23; ulcerovegetating, 17; scrofuloderma, 26; local tumors, 2; tuberculids, 21. Definite cure of lupus vulgaris was rare before the introduction of Charpy's method; since its introduction, about one-third of the patients are cured, one-third are apparently cured but have relapses, and one-third are not im-

proved. Charpy's method brings about clinical stabilization rather than genuine biological cure. Fair results are obtained with streptomycin alone or in combination with *p*-aminosalicylic acid and other agents. The author began to use these forms of treatment successively two years ago and has since obtained a higher proportion (55%) of complete cures than he did by either method alone. His technique consists of an initial treatment with antibiotics (1 gm. of streptomycin with 15 to 20 gm. of *p*-aminosalicylic acid daily) for two months, followed by treatment with vitamin D₂ (calciferol), one 15-mg. ampule of "sterogyl" every week, for six months. Cure is apparently brought about by the walling-off of the tuberculous areas by fibrosis. This process seems to be the same whether it takes place spontaneously or as a result of the administration of vitamin D₂ or antibiotics. Large doses of vitamin D₂ play a major part in the treatment of lupus vulgaris; nonlupous conditions benefit more from streptomycin and *p*-aminosalicylic acid. The successive use of these drugs, however, produces the largest proportion of cures in all forms of cutaneous tuberculosis.

Proceedings of Royal Society of Medicine, London

44:905-982 (Nov.) 1951. Partial Index

- Epidemiological Aspects of Work of World Health Organization. Y. Biraud.—p. 905.
- Abnormal Function of Upper Urinary Tract. J. C. Anderson.—p. 925.
- Psychosomatic Medicine and Psychotherapy. E. Kretschmer.—p. 965.
- Some Biochemical Aspects of Hypoglycaemic Coma. A. S. Thorley and W. W. Kay.—p. 969.

Schweizerische medizinische Wochenschrift, Basel

81:1141-1164 (Nov. 24) 1951. Partial Index

- *Masked Iron Deficiency, a Significant Factor in Patients with Dumping Syndrome After Gastrectomy. B. Jasiński and W. Ott.—p. 1141.
- Nosology of Epicondylitis Humeri Lateralis. W. Belart.—p. 1145.
- Significance of Carboxylase for Metabolism and Treatment. S. Markeset.—p. 1145.

Iron Deficiency in Dumping Syndrome After Gastrectomy.—The authors investigated the iron metabolism of 39 patients with the postgastrectomy dumping syndrome and of 6 patients with peptic ulcer who complained of fatigue, headache, palpitation, and other symptoms not characteristic of peptic ulcer. They reasoned that the symptoms in all these patients might be due to an iron deficiency since: (1) patients with peptic ulcer have chronic blood loss before operation, (2) resection of the stomach alters the anatomic and physiologic conditions in the upper gastrointestinal tract so that absorption and reabsorption of ordinary amounts of iron from food are interfered with, and (3) the resultant iron deficiency may produce symptoms by interfering with tissue metabolism, through a reduction in iron-containing cytochrome and ferritin without producing a significant decrease in hemoglobin. Their studies confirmed their suspicions. With three exceptions their patients did not have frank anemia, and most of them had normal fasting serum levels, but 40 of the 45 had abnormal responses to the iron tolerance test. In this test eight 0.2 gm. tablets of ferrous gluconate (176 mg. of iron) are given orally to the fasting patient and the iron content of the serum is determined before and one, three, and seven hours after the injection. Normally there is little or no evidence of iron absorption, but in iron deficient patients the serum iron level rises sharply. In this series all but five patients showed pronounced increases in serum iron to levels of 200 to 300 γ per 100 cc. Iron therapy then was instituted with 2 tablets of ferrous gluconate three times daily for three months. Complete freedom from symptoms, including disappearance of refractory diarrhea, resulted in 14 patients. Fatigue, headache, and palpitation disappeared gradually in an additional 15 patients. The remaining patients were therapeutic failures. The iron metabolism of patients subjected to gastrectomy and of patients with peptic ulcer should be studied carefully. If gastrectomy is performed during the phase of negative iron balance, one may assume that iron deficiency disease will develop with a dumping syndrome as its clinical manifestation. The incidence of the dumping syndrome, the mechanism of which is still poorly understood, may be decreased by attention to this factor.

BOOK REVIEWS

Health in Schools. Twentieth Yearbook. Second edition. Cloth. \$4. Pp. 477, with illustrations. American Association of School Administrators, department of National Education Association of United States, 1201 16th St., N.W., Washington 6, D. C., 1951.

As is suggested in the foreword, this volume is an important companion piece for "Health Education," in which the N. E. A. also has a part, not only because it provides necessary information for school administration but also because it completely orients administrators to school health matters that might otherwise remain exclusively at the teaching level. The special commission responsible for this extensively revised edition is composed of top flight workers in education and health education, who had the assistance of other highly qualified persons from related fields, such as physical education and dentistry. The result is a volume that provides background and recommendations that the administrator can put to practical, profitable use.

Proceeding from the general to the specific, the volume considers the overall problem in two preliminary chapters and then gives detailed attention to major topics, including school environment, mental health, physical education, health appraisal and counseling, communicable and noncommunicable diseases, school health emergencies, and the consolidation of school and community interests in health activities. There is a special chapter on sources and resources that contains a wealth of suggestions, with each chapter of the book treated from this angle. There is also a special section listing government and private agencies from which related material or information can be obtained. In a novel final three-page discussion headed "Mr. Superintendent—Your Health," administrators are reminded that they too are only human. Each chapter concludes with a list of selected references and a page of pointed questions that drive home the main ideas considered in the chapter. In the introduction, John L. Bracken, who was chairman of the commission that prepared the last Yearbook in 1942, analyzes the changing situation and the important contributions of this new edition.

Autopsy Diagnosis and Technique. By Otto Saphir, M.D., Clinical Professor of Pathology, University of Illinois Medical School, Chicago. Foreword by Ludvig Hektoen, M.D. Third edition. Cloth. \$6. Pp. 471, with 80 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1951.

This popular book not only deals with the technique and legal implications of autopsy but also provides useful information concerning the diagnosis and evaluation of autopsy observations. It is a valuable supplement to the standard textbooks of pathology, and can be of great help to the beginner who is looking for quick orientation and guidance in a confusing field. Each region of the body is considered separately. The author's clear and facile diction in dealing with a dry subject deserves special comment. The book has proved its value to the student, to the practitioner who is occasionally called upon to perform an autopsy, and to the young pathologist, as evidenced by its appearance in a revised and enlarged third edition. Consideration of morphological characteristics in pathological diagnosis and establishment of the cause of death is emphasized more in this edition than in previous ones. New knowledge in the field of pathology, especially in endocrine, renal, and bone diseases, is fully considered. In addition to recommended dissection by removal of organ systems *in toto*, a modified Virchow's method of removal and dissection of individual organs is also described. Performance of autopsies on embalmed and decomposed bodies is discussed. The author has included a chapter on practical suggestions for quick orientation. This edition is even more commendable than the previous ones, and it deserves to be read by everyone concerned with performance of autopsies and interpretation of autopsy observations.

Cost of Medical Care: The Expenditures for Medical Care of 455 Families in the San Francisco Bay Area, 1947-1948. By Emily H. Huntington. Issued under auspices of Heller Committee for Research in Social Economics, University of California. Paper. \$2.50. Pp. 146. University of California Press, Berkeley 4; Cambridge University Press, Bentley House, 200 Euston Rd., London, N.W.1, 1951.

The Heller Committee for Research in Social Economics of the University of California has presented a study of the expenditures for medical care of 455 moderate income families in the San Francisco Bay area in 1947-1948. After extensive analysis of the expenditures for medical care, the composition of the families, the illnesses for which medical care was required, the types of medical care required, and the amount of prepayment coverage, this report concludes that expenditures for medical care can be burdensome and sometimes disastrous and that "the only way that real protection can be accomplished is through a system of compulsory health insurance at least for the low- and moderate-income groups in our population."

This conclusion is not supported by the findings of the study. The great majority of the families studied had medical expenditures that could not be called disastrous in relation to their income. The most common illnesses were colds and influenza. In approximately 75% of the reported illnesses the bill was less than \$50. Childbirth costs were the largest single item of medical expense for the group as a whole as well as for those families in which a child was born during the year.

The author states that while 60% of the families had some form of health insurance, voluntary insurance was inadequate because its coverage was concentrated on hospitalized illness. Two-thirds of the families with health insurance were covered for hospitalized illness. The study, however, shows that the hospitalized illnesses are the costly ones for which families want protection. Seventy per cent of the costly illnesses were hospitalized in contrast with only about 10% of all illnesses. The report states, "the more expensive illnesses were those most likely to receive prepaid care." Of course, it is desirable that other medical costs be covered, but in something as new as the development of voluntary health insurance, it is only logical that the first plans introduced would be designed to meet the costs of the most burdensome illnesses. More and more plans offering other types of health insurance are being introduced. In fact, since 1947, the first year during which the Heller study was conducted, hospitalization coverage in the United States has increased 46%, surgical coverage 108%, and medical coverage 143%. On the basis of these figures and on the basis of the findings of the Heller report itself, the author is hardly justified in stating that "voluntary health insurance has been tried and found wanting, and that it is not likely in the future to give insurance protection to those who need it most." On the contrary, it has proved to be the most effective method of meeting medical costs, and it is rapidly reaching more and more individuals. It is unfortunate that the conclusions of the author are inconsistent with the study itself, since the study does contain valuable information that could greatly contribute to the literature on medical care costs.

A Manual of Orthoptics. By Julia E. Lancaster, M.A. Cloth. \$5.50. Pp. 199. Charles C Thomas, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, 1951.

Written by one of America's leading orthoptic technicians, this book brings a sane, conservative viewpoint into the field of orthoptics. It should do much to bridge the gap between the orthoptic nihilists and those whose overenthusiastic optimism has brought discredit to the entire field of fusion training. For the diagnosis of various forms of muscular imbalance and for indications for their surgical correction, the reader is referred to standard textbooks on ophthalmology. The author wisely confines herself to the psychological and technical aspects of the subject that must be mastered by the successful technician.

Orthoptics is defined as "that portion of ophthalmology which deals with helping the patient to get the best possible use of his

two eyes." Great emphasis is placed on the establishment of rapport between the child and the technician. The latter must understand the mental processes of the patient as related to orthoptic progress. The first part of the book, dealing largely with philosophical and psychological aspects, reveals a depth of understanding that could be studied with profit by members of any profession who work with children. The second part of the book is concerned with techniques and has chapters on orthoptic analysis, breaking down suppression, teaching convergence control, teaching divergence control, accommodative squint, anomalous correspondence, and orthoptics for adults. This volume should be required reading for every orthoptic technician. The ophthalmologist will find in it a better understanding of the true place of orthoptics as an ophthalmologic adjunct.

Immuno-Catalysis and Related Fields of Bacteriology and Biochemistry. By M. G. Sevag, Ph.D., Associate Professor, Department of Bacteriology, School of Medicine, University of Pennsylvania, Philadelphia. With preface by Stuart Mudd, M.A., M.D., Professor of Bacteriology, School of Medicine, University of Pennsylvania. Second edition. Cloth. \$12. Pp. 547, with illustrations. Charles C Thomas, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, 1951.

Interrelationships between phenomena of immunity and biocatalysis have been noted for some years. In fact, Ehrlich derived his famous lock and key simile for the expression of the specificity of antibody with respect to antigen from enzyme specificity studies of Emil Fischer. In general, however, workers in the field of enzymology have given little, if any, consideration to the possible relations among the fields of biochemistry, immunology, and bacteriology. The fullness of integration among these fields is indicated for the first time in this text. Specialists in either enzymology or immunology will consider the first three sections of this book to be a reservoir of experimental facts, considered with insight and interrelated with remarkable synthesis. The pharmacologically active enzymes indigenous to plants, pathogenic bacteria, and snake venoms are considered in detail, with references to the relation between their chemical activities in vitro and their pharmacodynamic actions in vivo. The production of a specific immunity considered against this array of data leads the reader to the conclusion that many of the diverse symptoms and lesions of infectious diseases can be explained in terms of the actions of biocatalysts. In fact, the present tendency is to explain these symptoms as special manifestations of enzyme action. The many recent chemical and pharmacologic studies with lecithinases, proteases, and nucleases of snake venom are only a few of the more pertinent indications of this trend.

Teachers and investigators concerned with the mechanisms involved in infectious diseases will find in this work an augmented source of information. There has been no apparent attempt to restrict or limit the use of references; these are grouped in a bibliography at the end of the book.

Essentials of Pharmacology. By Frances K. Oldham, Ph.D., M.D., Research Associate in Pharmacology, University of Chicago, Chicago, F. E. Kelsey, Ph.D., Associate Professor of Pharmacology, University of Chicago, and E. M. K. Geiling, Ph.D., M.D., Frank P. Hixon Distinguished Service Professor and Chairman of Department of Pharmacology, University of Chicago. Second edition. Cloth. \$5. Pp. 462, with illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; Aldine House, 10-13 Bedford St., London, W.C.2; 2083 Guy St., Montreal 1951.

This edition of this introductory text in pharmacology is similar in purpose and style to the first. The new edition differs from the old chiefly in that recent changes in the field have been included, necessitating, particularly, revision of the material on autonomic blocking drugs, antibiotics, antihistaminics, and radioactive isotopes. The authors discuss the subject material of a course in pharmacology directed to medical students or practicing physicians. To accomplish this, they have omitted much of the fundamental material relating to pharmacologic principles as well as to the pharmacodynamics of most drugs. In the preface they admit to this shortcoming and state that for such details the reader must look elsewhere. In most instances satisfactory references are given to pertinent review articles or pub-

lications. There are a number of typographical errors in the book, and there is a lack of consistency in the use of synonymous drug names that is apt to cause some confusion; however, in spite of these criticisms, the volume provides a brief survey in pharmacology that should be of value to the student or physician.

Pathology of the Fetus and the Newborn. By Edith L. Potter, M.D., Ph.D., Associate Professor of Pathology, Department of Obstetrics and Gynecology, University of Chicago, Chicago. Cloth. \$19. Pp. 574, with 601 illustrations. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1952.

Dr. Potter is interested in the fetus as it develops in the uterus and in the infant as it adapts, after birth, to a new environment and a new type of existence. During the time that material for this book was collected, over 6,000 autopsies were performed at the Chicago Lying-in Hospital on infants and fetuses that died in that hospital and other places; tissues from over 3,000 additional autopsies performed elsewhere by pathologists from the Chicago Department of Health were also examined.

Dr. Potter points out that the pathology of the fetus and young infant has, until recently, been neglected. The pathological changes that occur during the infant's brief life are often meager and are sometimes overlooked by the inexperienced investigator. This volume was prepared to help those who are attempting to discover the causes of nonsurvival and to stimulate interest in those who have the opportunity and the material with which to work. There are 28 chapters that cover every aspect of the pathology of the fetus and the newborn infant.

It is difficult to analyze individual chapters, because they are all important. The author has covered her subject so completely and so accurately that no serious error can be detected. The vast amount of material is discussed in an interesting style. At the end of each chapter, there is an excellent list of references. On the whole, the book is an outstanding accomplishment and will remain a classic for many years. The publishers also are to be highly complimented. The paper is of excellent quality; the type is clear; the illustrations are beautifully reproduced; and the binding is sturdy. This book will be valuable to obstetricians, pediatricians, pathologists, and teratologists.

A Textbook of Medicine. Edited by Russell L. Cecil, M.D., Sc.D., and Robert F. Loeb, M.D., Bard Professor of Medicine, Columbia University, New York. Associate editors: Alexander B. Gutman, M.D., Professor of Medicine, Columbia University, New York, Walsh McDermott, M.D., Associate Professor of Medicine, Cornell University, New York, Harold G. Wolff, M.D., Associate Professor of Medicine (Neurology), Cornell University, New York. Eighth edition. Cloth. \$12. Pp. 1627, with 204 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1951.

This is a thoroughly revised edition of one of the classical teaching textbooks of medicine. The editors have accomplished the seemingly impossible task of including more subject matter, in the form of twenty new treatises, and shortening the text by 8%. This has been accomplished by the complete rewriting of many sections. Diseases have been regrouped according to etiology and the basic physiological, biochemical, and pathological factors discussed. Psychosomatic aspects are not neglected. Therapeutics are conservatively and generally handled. This is a thoroughly satisfactory textbook of medicine, excellent for teaching medical students or as a ready standard reference volume for the physician.

From Dugout to Hilltop. By Margaret R. Stewart, M.D. Cloth. \$3.75. Pp. 233. Murray & Gee, Inc., Culver City, Calif., 1951.

This is the autobiography of one of America's pioneer women physicians, the first woman to be commissioned by the Public Health Service and the first woman to attain the rank of senior surgeon. Particularly interesting are the early chapters in which the author describes her mother's struggle to raise a large brood of children on a Nebraska homestead. Other chapters describe her experiences in medical school and internship in California, and during her post-graduate study at the Women's Medical College of Pennsylvania, her private practice in the West, and her 25 years in government service.

QUERIES AND MINOR NOTES

PAINFUL FEET

TO THE EDITOR:—For many years I have had pain over the heads of my metatarsals and have been able to stand for decreasing periods of time. There is a callus under my second metatarsophalangeal joint, and that is where most of the pain is. I have tried bars and arch supports with slight relief. Standing causes pain, but when walking, I have very little pain. Recently I stood for a whole day on a concrete floor that was covered with sand to a depth of an inch or more, but when it became necessary to remove the sand, my feet immediately became painful. Crepe-soled shoes afford considerable relief, and if a felt lift is added under the great toes the relief is increased. I have two pairs of shoes that have crepe soles, and they have a soft, plastic substance in the insoles, which have molded to my feet and have hardened. When wearing these shoes, I am relieved of some pain, but I can not wear them for office use, and I am unable to find another pair of shoes with this substance in the insoles. Can you tell me where I can get this kind of shoe? This is a serious condition, and any help will be appreciated.

M.D., Texas.

ANSWER.—The description of the symptoms suggests a metatarsalgia with a painful callus associated with pes valgo planus. This is usually secondary to foot strain of long standing. Having a shoe that fits exactly to the foot does give relief, but offers no means of improving the condition. To correct the condition, it would be necessary to bring the foot into normal position and to learn to use it normally again. (See Hauser, E. D. S.: Diseases of the Foot, Philadelphia, W. B. Saunders Company, 1939, pp. 48, 65.) The form fitting type of shoe is made commercially by the Conformal Shoe Company, 1509 Washington Ave., St. Louis 3, Mo.

SYPHILOPHOBIA

TO THE EDITOR:—A 30-year-old white man has been in perfect health all his life. He has been married for six years, and his blood test was negative prior to marriage. In May, he had extramarital sexual intercourse with a girl who allegedly infected two men at that time. Since early June, he claims to have soreness around his genitalia and in his mouth. The three physicians who examined him found no physical manifestations of any venereal disease, and all three made blood tests with negative results, the last one being made late in July. On August 5, he was examined again and found to be completely normal; his blood test (Kahn qualitative) was also negative. Is it advisable to treat this man prophylactically after his contact has been found to be infected with syphilis, even though this cannot be determined for several weeks? If this man does not insist on prophylactic treatment, is it permissible to omit treatment and have him observed for lesions and serologic blood tests? O. Hoke, M.D., Durham, N. C.

ANSWER.—This man apparently has syphilophobia, with the development of so-called conscious symptoms: the soreness in the mouth and genitalia. The basis for this view is that had he acquired syphilis after exposure in May, there ordinarily would have been some sign of it by August. Therefore, antisiphilitic treatment is not required. However, he should be examined at frequent intervals for some months; at the same time every effort should be made to rid him of his fears. There are some physicians who feel that if such efforts fail, he might be given treatment with repository penicillin for early syphilis as a psychotherapeutic measure, provided there is some chance that this treatment will eradicate his phobia. Others suggest that placebo injections of sterile water would be equally effective.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

CHROMIUM DERMATITIS

TO THE EDITOR:—Is there any protective or preventive measure against the irritant effect on the hands caused by the chromic acid preparation used in the engraving industry? It produces dermatitis venenata with blisters and pruritis. Gloves cannot be used, since fine stencil work must be done in the process. Would an ointment or preparation of BAL be effective? Can one be desensitized to the chromic acid preparation causing the irritation? Is there an agent that, when applied to the hands, will leave a residue capable of neutralizing the ill-effects of the irritant?

Bernard J. Schaffer, M.D., Chicago, Ill.

ANSWER.—Skin protection in the employment described is difficult, since ordinary water-repelling greasy barrier creams transfer fingerprints to the product. The chromium compounds utilized are oxidized with difficulty. The best approach is through frequent lavings in weak reducing agents, such as a 5% sodium hyposulfite solution. A weak ascorbic acid solution may be still better. The Lithographic Technical Foundation (1800 S. Prairie Ave., Chicago 16) has long advocated the application of weak solutions of citrates and tartrates. While chromates will attack the unbroken skin, the injured skin is far more vulnerable. No worker with open skin lesions should be permitted to undergo exposure. Individual susceptibility and sensitization are important. Planned desensitization is rarely practical, but spontaneous desensitization occurs commonly. By no means are all chromium compounds equally active in irritant properties. Valence determines degree of possible damage.

TESTOSTERONE AND CHRONIC PROSTATITIS

TO THE EDITOR:—A white man, 35 years old, has chronic prostatitis. For one year previously, he has been given testosterone at monthly intervals, by injection. The dosage is not known. What is the effect of the testosterone on the prostate gland from the physiological and cytological standpoints? Would continued use of testosterone alter his libido? A complete urologic examination, including cystoscopy with retrograde studies, revealed only chronic prostatitis.

Frank M. Hilpert, M.D., Racine, Wis.

ANSWER.—Testosterone has little or no effect on the physiology or cytology of the prostate gland of a noncastrated male, 35 years old. It is of no value in the treatment of chronic prostatitis. It is not clearly stated whether the patient's libido is decreased, but, if so, the administration of testosterone in a man of this age with normal testicular function usually does not restore it. Impotency in a normal young man usually is dependent on psychological factors and is not caused by chronic inflammation of the prostate gland.

TACHYCARDIA AND ANTIHISTAMINES

TO THE EDITOR:—I have noticed extreme tachycardia in young persons who have taken antihistamine preparations, seasonally, for several years, for hay fever. Extensive cardiac study revealed no abnormality. Is this a coincidence or a result of the antihistamines?

Donald F. DeMoose, M.D., Holbrook, Ariz.

ANSWER.—The chief effect of the antihistamines on the cardiovascular system is that of excitation. Tachycardia and palpitation are commonly observed after the excessive or prolonged use of these drugs. Excitatory phenomena are especially likely to occur in children, young adults, and in highly nervous persons. Precordial distress and arrhythmia have also been observed. Mackmull, G. (J. Allergy 19:365 [Nov.] 1948), in studying the effect of diphenhydramine (benadryl®) hydrochloride administered intravenously to normal subjects, reported electrocardiographic changes of significance following the intravenous administration of 200 to 300 mg. of the drug.

TREATMENT OF MYOPIA

TO THE EDITOR:—After administration of a cycloplegic, the following results were obtained. The corrections that subjectively gave the best reading for a 9-year-old girl were right eye, 2.25 sph. and left eye, 1.50 sph. The most favorable corrections for an 11-year-old girl were right eye, 1.00 sph., and left eye, 1.00 sph. These girls have never worn glasses. Should their vision be corrected? If so, should they be given the correction that will enable them to read a poor 20/20? Should they wear glasses most of the time or just for distance? Are there any therapeutic suggestions other than glasses?

Richard L. Fruin, M.D., Inyokern, Calif.

ANSWER.—The vision of these patients should be corrected to a good 20/15 if possible, not a poor 20/20, and glasses should be worn for both distance and near work. If the myopia is fully corrected, the eye is artificially emmetropic. Without corrective lenses, the myopic eye accommodates very little, if at all. With corrective lenses, accommodation is necessary for looking at near objects. Accommodating may cause the patient some difficulty for near work, and the glasses may be removed because it is more comfortable to read without them. This feeling will pass. Removal of the lenses for near work defeats their purpose. Forcing the myopic eye to accommodate encourages the use of the ciliary muscle, which is essential for the proper physiological action of the eye; therefore, the lenses should be worn for both distance and near work.

Only corrective lenses will alleviate the symptoms of non-pathological myopia, which is due to the natural growth and development of the body. In the cases mentioned, it would be of interest to note the refractive states one year ago and compare the increase or decrease of the myopia. Aside from glasses, there are no therapeutic suggestions except good ocular hygiene, the use of adequate lighting, good reading habits, proper diet, and the maintenance of good health.

CHEST PAIN AND ANGINA PECTORIS

TO THE EDITOR:—Since last February, a man, aged 31, has had four attacks of a knife-like pain in his chest running down the left arm, associated with pallor and nausea. A shock-like condition does not exist. Blood pressure remains 120/80, pulse normal; electrocardiograms have been negative. The only other finding is tenderness in the left intercostal space. A specialist told him he has angina pectoris, although his electrocardiogram is negative, and has told him to remain in bed for six months to a year, with absolutely no activity. The specialist advised the patient to carry a flask of whiskey with him and to take some whenever he feels an attack coming on. I would appreciate your opinion.

Michael J. Lavin, M.D., Pontiac, Ill.

ANSWER.—The symptoms are not typical of angina pectoris. More details of the symptoms, however, are of importance; for example, at what times the pain is present, that is, whether on effort, at rest, on excitement, or in relation to meals. However, a normal electrocardiogram does not rule out coronary heart disease. An exercise test might be of some additional value. More extensive study to look for factors other than coronary heart disease to explain this pain would seem to be warranted.

DRYNESS OF VAGINA

TO THE EDITOR:—A registered nurse, aged 30, complains of extreme dryness of the vagina, which began three months ago. She is the mother of two children, both delivered by cesarean section. There is nothing abnormal about her menses. The only time she notices this dryness is during intercourse, and then there is no pain, only diminished sensation. She has stopped taking douches. What could cause this sudden drying of the vaginal mucosa?

M.D., Arkansas.

ANSWER.—In the absence of physical reasons for drying, that is, prolapse and relaxation, and in the absence of any drug being administered that might cause drying, reasons connected with intercourse should be suspected, namely, disinterest or failure to be properly stimulated to cause mucus secretion. In any event, if the dryness occurs only during intercourse, a small amount of lubricating jelly will usually solve the problem.

TOTAL ALOPECIA IN A CHILD

TO THE EDITOR:—A boy, 8 years old, had a normal birth, and when he was 2 years old had a full head of hair and normal eyebrows. Now he is of average size, well nourished, has no apparent glandular defects, and has a normal I. Q. Six years ago, shortly after his mother was desperately ill with pneumonia, his hair and eyebrows began falling out, and, in a few months, he had total alopecia. His scalp has the sheen of the bald head with no hair follicles seen. Everything has been done without results. A specialist made a diagnosis of shock from his mother's severe illness as the cause. Can you suggest cause and treatment?

O. W. Ridgeway, M.D., Indianapolis, Ind.

ANSWER.—There is no specific treatment for alopecia totalis, nor is there a known cause. Emotional disturbances and alopecia areata occur together so frequently that the connection cannot be disregarded. The condition may have begun as ordinary alopecia areata, and infants and children do have emotional disturbances. Endocrine abnormalities, foci of infection, visual defects, and nutritional disturbances have long been suspected, but never established, as causative factors. The prognosis is poor. Psychotherapy and stimulating measures are occasionally effective. Ultraviolet rays, massage, and vasodilating agents, such as nicotinic acid and ointments containing ammoniated mercury or histamine, are the treatments frequently employed. Permanent regrowth of hair is said to occur in about 3% of the cases.

INTERMITTENT SWELLING OF CHEEK

TO THE EDITOR:—A 44-year-old white woman has an intermittent swelling of the right cheek. The swelling is diffuse, more pronounced on the inside, and involves the entire right cheek. The only symptom produced is a feeling of tightness in that side. It appears suddenly and lasts for varying lengths of time; however, slight fullness seems to be there at all times. This situation has existed for several months. The patient had two small calculi removed from the right submaxillary gland a few weeks prior to the onset of this swelling. She recently had an infected upper left molar tooth removed. She is now having symptoms suggesting the onset of menopause. A few years ago she was found to have a gastrointestinal allergy to certain foods. She is emotional, highstrung, and occasionally overindulges in alcohol. She also has a benign essential hypertension. Can you suggest therapy or diagnostic measures?

L. C. Bailes, M.D., Anderson, S. C.

ANSWER.—The previous occurrence of calculi in a salivary gland and the behavior of the present swellings lead one to think that obstruction of the parotid gland duct by inflammation or calculus is the most likely diagnosis. Theoretically at least, it might also be possible for edema of the duct or the gland itself to be produced by an allergic reaction, which would most likely be due to a food. If other features of the case not presented in the query do not fit in with these possibilities, an angioneurotic edema of the buccal tissues may be considered. Skin tests with foods may yield a clue in such an event, but trial diets would be more reliable and direct. It is recommended that a diet containing only wheat and egg and milk products be used for about 10 days. If no relief ensues, the opposite diet, that is, a wheat-egg-milk-free diet, should be tried. If either diet improves the condition, additions can be made at about three day intervals.

TREATMENT OF CHRONIC LYMPHEDEMA

TO THE EDITOR:—A patient, 45 years of age, had a subtotal hysterectomy in 1942. Acute thrombophlebitis of the left leg developed during her convalescence. Lymphedema has persisted since then. Can you suggest treatment?

R. W. Kispert, M.D., Green Bay, Wis.

ANSWER.—At this late phase, only simple palliative measures would be beneficial. Persisting lymphedema is a frequent sequel, leaving one leg definitely larger than the other. Paravertebral sympathectomy, which often improves the circulation in the early stages, would have little value now. Such patients usually get along comfortably by keeping the limb elevated when sitting, wearing light-weight elastic stockings, taking massage, and avoiding trauma, which might produce ulceration of the limb.

MANAGEMENT OF ACUTE DISORDERS OF THE BILIARY TRACT

William D. Holden, M.D., Frank A. Cebul, M.D.

and

Charles W. Loughry, M.D., Cleveland

Two years ago, Ogilvie,¹ in an address to the Western Surgical Association, stated that he had never seen a case of acute cholecystitis in which the gallbladder burst, nor had he heard of one in the wards of the hospital in which he had worked for 40 years. This is a rather striking statement from a surgeon with his experience, and it was used as part of his criticism of early cholecystectomy for acute cholecystitis.

There is no doubt that there has been a tremendous interest in this subject among the members of the medical profession in this country during the last 20 years. A good number of surgeons have advocated early operation in acute cholecystitis and have presented statistical data to corroborate and implement their proposal. This has provoked but a small amount of criticism. It becomes important to determine, now that several years have elapsed since early cholecystectomy for acute cholecystitis was instituted, whether or not it is to the patient's best interest. The thesis that all acute conditions should be subjected to early operation, as acute appendicitis is managed, or that there are factors characteristic of each patient which permit a selected disposition of the problem, should be scrutinized with care. It is often difficult to obtain valid answers to such a question, especially when the mortality for the surgical treatment has attained such low levels. Other factors, such as hospital morbidity, recurrent operations, and complications, must be utilized in evaluation of the desirability and propriety of adhering to the proposal.

It also becomes necessary to understand, in so far as we are able, what is meant by the term "acute cholecystitis." It is a term used loosely by clinicians and pathologists as well.

It also becomes of importance to determine whether the proposal that early cholecystectomy for acute cholecystitis is as desirable in all the hospitals of the country as it may be in the large medical centers. What may be

of great value to one segment of the medical profession may not necessarily be of equal worth to another segment, because of different circumstances.

The following discussion may or may not be of assistance in clarifying the problem of caring for the patient with acute inflammation of the gallbladder. Many of the statements are at variance with generally accepted ones and may provoke discussion that will further elucidate this controversial problem.

One of the first to advance the hypothesis that early operation should be performed was Miller² (1930). He stated, "In the presence of definite subsidence of symptoms and signs of which the surgeon is sure, and with the patient's condition good, operation may be safely put off. If, on the other hand, there is a persistence of temperature, tenderness, and spasm, and particularly and most important, if there is severe pain not easily controlled, surgical intervention should be undertaken without delay." This proposal appears reasonable, but the success of carrying it out depends on careful and frequent observation of the patient's course over a period of at least eight hours. Generally speaking, this is possible in almost any community in the country. Certainly a patient for whom a diagnosis of acute appendicitis is being entertained, but cannot definitely be made, is observed frequently enough to permit operation if the diagnosis of acute appendicitis becomes apparent. There is little reason why the patient with acute inflammation of the gallbladder should not be observed as carefully. Some patients will require early operation, and these can be differentiated from those who can be subjected to subsequent elective cholecystectomy. Perhaps it is rash to make such a statement, for many surgeons have clearly stated their inability to do so. After Miller had advocated a more vigorous attitude toward the management of acute cholecystitis, a good many surgeons³ during the early thirties presented the hypoth-

From the Department of Surgery, Western Reserve University School of Medicine and University Hospitals of Cleveland.

Read before the General Scientific Meetings at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 11, 1951.

1. Ogilvie, H.: Men of Two Worlds, *Arch. Surg.* 61: 7, 1950.

2. Miller, R. H.: Acute Cholecystitis, *Ann. Surg.* 92: 644, 1930.

3. Heuer, G. I.: Factors Leading to Death in Operations upon Gall-Bladder and Bile-Ducts, *Ann. Surg.* 99: 881-892, 1934. Graham, H. F., and Waters, H. S.: Important Factors in Surgical Treatment of Cholecystitis, *ibid.* 99: 893, 1934. Touroff, A. S. W.: Acute Cholecystitis: Study of 75 Proven Cases with Subsiding or Subsided Clinical Manifestations at Time of Operation, *ibid.* 99: 900, 1934.

esis that all acutely inflamed gallbladders should be removed as soon as the patient could be adequately prepared for the operation. The basis for the proposal was that, first, it was impossible to comprehend the pathologic process by observation of the clinical manifestations; second, perforation of the gallbladder could be avoided; and, third, the acutely inflamed gallbladder could be removed with little additional mortality than was associated with elective cholecystectomy for cholelithiasis.

Before considering the arguments that favor early cholecystectomy, it would be advisable to know what is meant by the term "acute cholecystitis." Is it a bacterial infection, a chemical irritation, or inflammation resulting from changes in the venous and lymphatic circulation of the gallbladder? There undoubtedly is more than one factor involved in different cases and at different

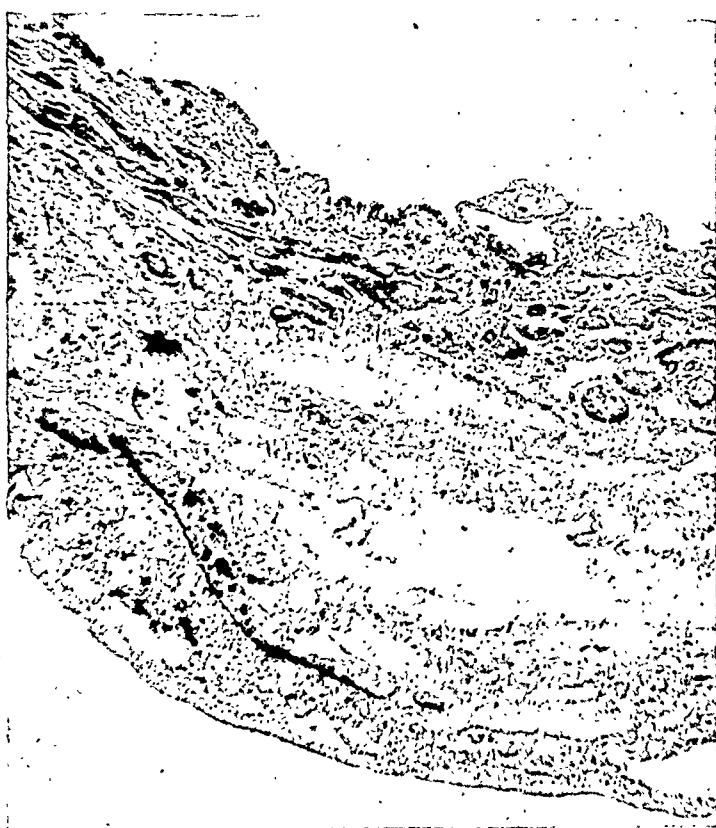


Fig. 1.—Wall of gallbladder. There is demonstrable distension of venous and lymphatic spaces and a considerable amount of edema. There are few inflammatory leukocytes, and the mucosa is within normal limits. The appearance suggests a vascular rather than a bacterial or chemical etiology.

times in the same patient. For a good many years, acute cholecystitis was thought to be a bacterial infection and various pathogenic organisms were cultured from either the contents or the wall of the gallbladder. Cultures were positive from the lumen only occasionally, except in frank empyema, and it was claimed that they were in the wall of the organ even when they could not be demonstrated in the lumen. In most of these cases, signs of an inflammatory lesion in the gallbladder had been present for several days or weeks prior to operation or death. These organisms may reach the gallbladder by several different routes, and there is no agreement as to which one is the most frequent or important. They may reach

the gallbladder through the blood stream, through the lymphatics from the duodenum or liver, and through the cystic duct. One of the major difficulties in accepting any theory concerning the role or importance of bacteria in the etiology of acute cholecystitis is the observation that the same organisms are found with about the same frequency in chronic cholecystitis. More frequently than not, no organisms can be cultured from any part of the gallbladder.

Acute inflammation of the gallbladder is practically always associated with obstruction to the flow of bile into the cystic duct by an impacted calculus. Concentration of the bile occurs under these circumstances, and a chemical inflammation of the mucosa and submucosa results. This situation does not invariably hold, because occasionally the acutely inflamed gallbladder can be readily emptied at the time of operation.

A stone impacted in the ampulla of the gallbladder may seriously compromise lymphatic and venous drainage without invariably interfering with the egress of bile through the cystic duct. In 1927, Denton⁴ observed that acute inflammatory changes in the wall of the gallbladder were always associated with the presence of calculi and that the early changes consisted of edema of the submucous and serous layers and venous distention demonstrable chiefly in the same layers (Fig. 1). More serious interference with the lymphatic and venous drainage produced ecchymotic areas in the wall of the gallbladder and eventually actual necrosis (Fig. 2). The fact that attacks of acute gallbladder pain almost always start suddenly, combined with Denton's observations, suggests that the sudden impaction of a stone in the ampulla or cystic duct is the primary pathogenic factor involved in acute inflammation of the gallbladder. If the egress of bile from the gallbladder is prevented, chemical inflammation and necrosis of the mucosa may be added, and, if obstruction persists long enough, pyogenic infection may be superimposed on already existing pathologic tissues.

Of what value is some knowledge of the vascular changes occurring in the gallbladder? Is not the observation of progressive necrosis of the wall of the gallbladder an argument in favor of early operation?

Knowledge of the vascular changes is of the greatest value in understanding the clinical manifestations. If it is borne in mind that acute inflammation of the gallbladder can progress with great rapidity because of the vascular component in the pathogenesis, it behooves the clinician to observe his patient frequently and carefully. Since up to a certain point the process is reversible if the calculus is dislodged from the site where it is producing its obstructing effect, the clinician can rely on the subsidence of colicky pain as an indication of imminent recovery. If the colicky pain becomes more intense and ultimately becomes a constant aching pain, then he should be aware of impending serious trouble.

The latter events in our experience rarely occur. Cowley and Harkins⁵ in 1943 found in a review of the literature that an average of 13% of the acute cases with perforation, or 2.8% of all cases, acute and chronic. These do not all represent free perforation into the peritoneal cavity. Among their own cases, numbering 2,750, there were 25 perforations, of which 6 were free,

4. Denton, J.: Mode of Origin of Gallbladder Lesions, *Arch. Surg.* 14: 1, 1927.

5. Cowley, L. L., and Harkins, H. N.: Perforation of the Gallbladder, *Surg., Gynec. & Obst.* 77: 661, 1943.

16 local, and 3 into an abdominal viscus. Only one of the patients with a free perforation died.

During a 10-year period (1940-1950), 1,523 cholecystectomies were performed at the University Hospitals of Cleveland. There were 20 perforations, of which 17 were local in character and three were free into the peritoneal cavity. By local perforation is meant the formation of a pericholecystic abscess or collection of bile. This represents an incidence of 1.3%. The three free perforations were encountered in acute cases, and in two of the three, so far as can be told, perforation had occurred before admission of the patient to the hospital. One of these patients died. Of the 17 localized perforations, 6 were found in acute cases and 11 in chronic. The total of 9 perforations in 315 acutely inflamed gallbladders represents an incidence of 2.8%.

There is little doubt that our conservatism in operating on a patient with acute inflammation of the gallbladder is due in large part to the low incidence of perforation that exists in our cases as well as the fact that only one patient in 1,523 died as a result of perforation.

Low mortality rates, ranging from 1.5% to 5.3%, for removal of the acutely inflamed gallbladder have been reported from several large institutions, and as

Mortality Among 1,523 Patients Subjected to Cholecystectomy

	No.	%
Over-all mortality	17	1.1
Acute inflammation	8	2.5
Chronic inflammation	9	0.74
Staff patients	6	1.7
Private patients	11	0.93
Under age 50.....	2	0.25
Over age 50.....	15	2.0

Buxton, Ray, and Coller⁶ pointed out recently it is questionable whether the low mortality rate can be ascribed to the operation or to better preoperative and postoperative care. An added factor is the increased amount of attention given these acutely ill patients during the past few years. In a large hospital with an adequate and alert resident staff, the patient is seen frequently, the operation is performed with an adequate operating room personnel, and considerable care is used in the prophylaxis of postoperative complications. The acutely inflamed gallbladder can be excised with a low mortality under these circumstances, but such do not universally exist.

In the series under discussion, 1,523 patients were subjected to cholecystectomy: 343 gallbladders were removed by the resident staff and 1,180 by the visiting staff; 315 of the gallbladders were acutely inflamed according to the histologic examination, and 1,208 were chronically inflamed.

The accompanying table shows the mortality for this group of patients. These mortality rates appear to be quite reasonable, and to a certain extent, which is difficult to estimate with any degree of accuracy, they are due to a process of individualizing the treatment of patients with biliary tract disease. Since 1945, four of the 17 deaths have occurred, which is a mortality rate of 0.5%. Three of the four occurred after removal of acutely inflamed gallbladders. One resulted from a

residual stone left in the common duct, and two were due to a severe gastric dilatation and ileus that failed to respond to all measures. The remaining patient died from a massive pulmonary embolus following an elective cholecystectomy for cholelithiasis and chronic cholecystitis.

There has been considerable doubt concerning the optimum time for excision of the acutely inflamed gallbladder. A good many surgeons⁷ have expressed the view that the most dangerous period was from the 4th to the 10th or 12th day following the onset of an acute attack. This period was delineated because of an apparent higher mortality rate associated with the operation and also because the technical difficulties encountered at the operating table appeared to be greatest during this



Fig. 2.—Wall of gallbladder. A moderate number of polymorphonuclear leukocytes and early infarction are present. Distended venous and lymphatic channels are seen.

time. On the other hand, others have advocated operation as soon as the patient is adequately hydrated and prepared, irrespective of the time elapsed from the onset of the attack. The patients with acute inflammation of the gallbladder in this series have been subjected to various therapeutic policies. Some have been operated on a few hours after admission, and others have been observed for several days. Of the eight patients who died after operation for acute cholecystitis, five were operated on within 72 hours of the onset of their illness.

An average of 4.3 days elapsed from the onset of an acute attack to the day of admission to the hospital, and an additional 5.7 days elapsed before operation, a total of 10 days. This theoretically is the worst possible time

6. Buxton, R. W., Ray, D. K., and Coller, F. A.: Acute Cholecystitis, *J. A. M. A.* 146: 301 (May 26) 1951.

7. Barksdale, J. W., and Johnston, H. H.: Acute Cholecystitis, *Ann. Surg.* 127: 816, 1948.

to subject the patient to operation; yet our mortality figures compare favorably with those of the groups that advocate operation within 48 hours of the onset of an attack, as soon as preparation is completed. Furthermore, it is difficult from this study to propose routine early operation to prevent the dreaded complication of perforation, both because most of the 20 perforations had occurred prior to admission and because only one of the 20 patients died as a result of the perforation itself. It is often stated that, if the diagnosis of acute cholecystitis can be made within the first 72 hours after the onset of an attack, cholecystectomy can be performed with technical facility. This is undoubtedly true in many instances principally because an edematous gallbladder can be freed from the liver with ease. When edema has occurred around the neck of the gallbladder—and it not uncommonly does—the difficulties in dissecting free the cystic duct and artery increase the hazards of the procedure by significant amounts. The apparent increasing number of postoperative strictures of the common duct may very well be due in part to the overly enthusiastic efforts of surgeons attempting to remove acutely inflamed gallbladders from edematous and hyperemic tissues. All surgeons who are to remove acute gallbladders do not perform biliary surgery day in and day out. It does seem reasonable that an operation performed when the tissues about the neck of the gallbladder are acutely inflamed will present more opportunities for damage to the hepatic or common ducts. Fortunately, no injuries occurred to the extrahepatic biliary ducts in these 315 patients. One of the principal reasons, however, is the fact that with only a few exceptions the operations were all performed by or under the supervision of six attending surgeons. It is felt very strongly that, if the patient presents increasingly obvious manifestations of peritoneal irritation, gressive enlargement, and tenderness of the gallbladder, increasing leukocytosis, a failure of the colicky pain to subside, or a failure of the fever and pulse rate to diminish after a period of adequate observation and hydration, then operation should be performed as soon as possible. If, on the other hand, none of these indications for operation exist, then it is to the patient's interest to have a more thorough investigation prior to operation. It has been noted previously that only two of the 17 deaths in this series of patients occurred under the age of 50 and all of the patients who died after removal of an acutely inflamed gallbladder were over the age of 50. Many of these patients undoubtedly would have died, but, if a longer period of time had been utilized to investigate the cardiorespiratory and renal systems, some of the deaths might have been avoided.

It has been stated at various times that the diagnosis of acute cholecystitis is relatively easy to make. Exception can readily be taken to this statement unless the writer specifies whether his diagnostic criteria are clinical or histologic. Gallbladder colic in itself is not necessarily associated with acute inflammation of the wall of the gallbladder. It is true that, if it persists long enough, inflammatory changes will often develop, principally as a result of impaired lymphatic and venous blood flow. If the physician or surgeon makes a diagnosis of acute

cholecystitis in every patient he sees with colicky right upper quadrant pain, he is misleading himself. In this series of patients a diagnosis of acute cholecystitis was made in 187 instances. The pathologist, however, corroborated the diagnosis only 125 times. In the remainder, or 62 times, no acute inflammation was encountered, although calculi were found in all the gallbladders. This does not speak very well for the surgeon's diagnostic ability, but, if it is recalled and emphasized that gallbladder colic per se does not necessarily mean that acute inflammation is present, the difference in clinical and histologic diagnosis becomes apparent. On the other hand, in this series of patients an acutely inflamed gallbladder was encountered 190 times when the preoperative diagnosis listed on the anesthetic record stated chronic cholecystitis and cholelithiasis. This discrepancy is also readily explained after a more thorough study of the record. With the exception of 12 patients for whom a preoperative diagnosis either of acute appendicitis or perforated peptic ulcer was made, these patients had, within the three-week period before admission, an attack of acute pain in the right upper abdominal quadrant or epigastrium, and in many, symptoms and signs of inflammation had persisted up to the time of operation. The surgeon would have been justified in anticipating an acutely inflamed gallbladder in most of these patients.

It has been claimed that the complications following a cholecystectomy for acute inflammation of the gallbladder are no more frequent or serious than those following elective cholecystectomy for chronic cholecystitis and cholelithiasis. This may very well be true if the patient is seen and operated on within 48 hours of the onset of his disease. The average length of time elapsing prior to admission is 4.3 days. The incidence of serious complications in this group of patients is 14.9%, whereas in the group subjected to elective cholecystectomy for chronic cholecystitis it is 6.8%. Among serious complications are included a residual common duct stone, wound disruption, postoperative intra-abdominal hemorrhage, temporary biliary fistula, acute gastric dilatation or severe ileus, deep venous thrombosis, pulmonary embolism, pneumonia, postoperative intra-abdominal abscess, coronary thrombosis, and peritonitis. Such postoperative disturbances as mild atelectasis, superficial wound infection, and temporary urinary retention are not included. Sixty-six per cent of all the complications occurred prior to 1946 and 34% since that time. The reduction in postoperative complications, however, has been due principally to a marked decrease in those following elective cholecystectomy for chronic cholecystitis, because the complication rate following cholecystectomy for acute inflammation is essentially the same for the two five-year periods. Acute gastric dilatation or severe ileus occurred in 5.7% of the acute cases and in only 1.0% of the chronic. This was the most striking difference in the occurrence of any complication in the two groups. It appears that a better knowledge of how to replace fluid and maintain electrolyte balance and of the use of antibiotics has not materially reduced the incidence or severity of the complications following operation for acute cholecystitis in this series. It may be argued that,

if the operation had been performed earlier, the occurrence of many of these complications might have been avoided. This cannot be denied on the basis of any clear-cut data; yet the tendency to operate on the acutely ill patient as early as is consistent with adequate preparation has been far more prevalent during the past five years than previously. In spite of this, the complications remain about the same.

The occurrence of acute gastric dilatation following cholecystectomy for acute cholecystitis is of great interest to us. It is generally recognized that this may follow any type of abdominal surgery but is more frequently anticipated after surgery of the biliary tract or splenectomy. When it occurred, there was no reason to believe that it was the result of peritonitis. In two patients who died as a result of this complication, no peritonitis was encountered when postmortem examinations were performed. This complication was seen but rarely on the staff service, where intragastric suction was maintained for at least 48 hours following the operation. Acute gastric dilatation or severe ileus occurred not infrequently when the patient persisted in removing an indwelling nasogastric tube or the attending surgeon was too willing to abide by his patient's objections to the tube.

Common duct exploration in the presence of acute inflammation presents a rather difficult problem to us. The common duct was opened in 57 of the 315 patients who had acute cholecystitis, an incidence of 18%. Stones were encountered and removed in 22 patients, an incidence of 38.6%. This admittedly is not a very satisfactory record. When one considers the additional technical difficulty involved, as well as the fact that complications become more frequent after the common duct has been explored, it is a matter of dismay, to say the least, to find calculi in no more than roughly 40% of the patients. Two explanations are available, however. In five instances, pancreatitis, either acute or chronic, was encountered at the time of the laparotomy, and the common duct was opened principally to eliminate the possibility of a small stone being impacted at the ampulla of Vater. The other explanation concerns the difficulty encountered in distinguishing a dilated common bile duct from an acutely inflamed one. In practically all instances, the decision to explore the common duct was made by a surgeon with considerable experience in biliary tract surgery. Inexperience cannot be used to explain the failure to find more common duct calculi. There will always be a certain number of common duct explorations that are unrewarding, because whenever an indication for exploration exists, the surgeon is justified in opening the duct rather than risking the possibility of leaving a calculus that may require a second operation, with a large amount of added technical difficulty and risk to the patient.

The problem of cholecystostomy is not being discussed here, principally because not enough data are available to draw any reasonable conclusions. There is, unfortunately, a conviction among many surgeons that they are technically inadequate at the operating table if they are forced to perform a cholecystostomy when they had planned to excise the gallbladder. This, of course, is not generally true, and every effort should be made to dis-

courage such an attitude. The occasion for electing to drain the acutely inflamed gallbladder and remove the stones certainly will not arise frequently; but, when the indications do exist, there should be no hesitation in simply draining the gallbladder, preferably with the use of a local anesthetic. In Glenn's last report⁸ on biliary surgery for acute inflammation of the gallbladder, 81 of 697 patients, or 11.6%, were subjected to a cholecystostomy. The indications for drainage are two in number: (1) when the patient is debilitated and for any number of reasons cannot be expected to tolerate prolonged general anesthesia, high spinal anesthesia, or anything more than a minimal amount of surgical trauma and (2) when it is obvious by inspection of the neck of the gallbladder at the time of operation that any attempt to dissect away the edematous areolar tissue around the cystic duct may well endanger the continuity of the hepatic or common bile ducts. When the patient has had repeated attacks of gallbladder colic in the past and is subjected to exploration during an acute attack, this tissue around the cystic duct and artery is apt to be not only edematous but fibrous, and dissection in the presence of these pathologic tissues is particularly dangerous. There is no complication of biliary surgery more unfortunate than a severed hepatic or common duct, and wisdom in every instance dictates that, if dissection of the cystic duct and artery is to be unusually difficult, it had better be postponed until the acute inflammation has subsided. This is not to be interpreted as a blanket endorsement for cholecystostomy, for, generally speaking, it is not a desirable operation since it only temporarily solves the patient's problem and in most instances leads to a second operation. When the above-mentioned indications are present, however, cholecystostomy is indeed preferable to cholecystectomy. When it is performed under these conditions, the mortality will be relatively high because of the severity of the patient's biliary tract disease and the associated disturbances that initially led to the choice of a cholecystostomy. There is little doubt, however, that, if cholecystectomies were routinely performed on these patients, the mortality rate would be prohibitive.

Any consideration of operative intervention for acute cholecystitis must take into account the means whereby the diagnosis is made. If it is a clinical diagnosis, then the term acute cholecystitis should be used very cautiously if at all. Ninety-two per cent of the 1,208 patients in this series who had elective cholecystectomies had had at least one attack in the past that could be called by all the clinical criteria available "acute cholecystitis." Although it is impossible to say with any degree of certainty, it is doubtful that most of such attacks were more than gallbladder colic associated with mild vascular inflammatory changes in the wall of the gallbladder. Some were certainly of a more serious character, but in only 11 instances was a local perforation ultimately found when laparotomy was performed. This argues in favor of modifying the hypothesis that all patients with acute cholecystitis, as diagnosed clinically, be subjected to laparotomy.

8. Glenn, F.: *Surgical Treatment of Acute Cholecystitis*, Surg., Gynec. & Obst. 90: 643, 1950.

It has been pointed out by surgeons for a good many years that many of the serious problems associated with acute inflammation of the biliary tract would become evanescent if more patients in whom gallstones were demonstrated were advised to undergo a cholecystectomy. The objection to this proposal has always been the fact that many patients at postmortem examination are found to have biliary calculi that have been asymptomatic during life. There is no doubt that some persons will for years have no serious symptoms that can be ascribed to gallbladder calculi, but, for those in whom symptoms develop, the danger of serious complications is great. In this series, the mortality rate for patients undergoing cholecystectomy under the age of 50 was 0.25%. The risk, disability, and discomfort associated with an elective cholecystectomy are of little consequence compared with the gravity of acute inflammation of the gallbladder, perforation, common duct calculi, obstructive jaundice, and the difficulties that arise at the operating table when visceral relationships are altered by severe inflammatory changes.

SUMMARY

The data presented here indicate that, contrary to the opinion of many, the diagnosis of acute cholecystitis is not readily made if one establishes histologic rather than clinical criteria for the diagnosis. Acute gallbladder colic is often mistakenly referred to as acute cholecystitis. Any study that concerns itself with acute cholecystitis should unequivocally establish either clinical or pathologic criteria, preferably the latter, if the reader is not to be confused and misled.

It has been stressed by many authors that acute inflammation of the gallbladder should be treated as acute appendicitis is commonly treated; namely, if the patient is seen within the first 72 hours after the onset of an attack, surgery should be resorted to; but if he is seen after a period, it should be postponed. Others have presented the thesis that all acutely inflamed gallbladders should be excised irrespective of the time interval following inception of the attack. Our experience in operating on these patients within the first 72 hours has been so small that it is impossible to advocate or criticize such surgery. The average length of time before these patients are admitted to this hospital is 4.3 days. The data and mortality figures presented here, when compared with those of the groups that routinely perform early cholecystectomy, are favorable and, if anything, indicate that, if the proper indications exist for performing either a cholecystectomy or cholecystostomy, the time intervening from the onset of the attack to the time when the operation is performed is of little consequence; also, any thesis that delineates a critical period during which surgery may or may not be carried out is not to the patient's best interest.

We cannot justifiably advocate the routine removal of all acutely inflamed gallbladders provided there is no contraindication. On the other hand, an acutely inflamed gallbladder should promptly be either drained or removed when the proper indications are present and no contraindication exists. These indications are increasing signs of peritoneal irritation, progressive enlargement and tenderness of the gallbladder, failure of colicky pain

to subside, increasing leukocytosis, and failure of fever and pulse rate to diminish. The length of time during which a patient may be observed before operation is decided on cannot be sharply defined. Some patients will require surgery a few hours after admission; in others the indications for operation may be apparent only after several days of observation. In most of the patients the clinical manifestations will subside. These patients cannot be observed by the physician or surgeon once a day without serious difficulties arising and complicating the management of the patient. They should be seen at least every four hours, if not more frequently, until the symptoms and signs begin to subside or the decision to operate is made.

Emergency cholecystectomy is a procedure of much greater magnitude than emergency appendectomy, and, if the operation can be postponed and performed as an elective one, the risk of injuring the extrahepatic ductal system will be less and the number and frequency of the complications will be smaller. It has been suggested that the frequency with which the common and hepatic bile ducts are injured during a cholecystectomy is increasing in this country, and the implication is that many of these injuries occur during attempted or completed cholecystectomies for acute inflammatory lesions. There is no proof available, to our knowledge, that this is so, and in this study no evidence is available to support such an impression. It does stand to reason, however, that the opportunities for injuring the ducts are greater when acute inflammation is present.

The most pertinent conclusion arrived at from this study is that, if more patients with demonstrable biliary calculi were advised to have an elective cholecystectomy, there would be little reason for discussing the ephemeral phase "acute cholecystitis."

Jaundice After Plasma Transfusion.—The incidence of homologous serum jaundice after transfusions with pooled plasma is sufficiently high (5-15%) that many have abandoned its use save for the emergency treatment of shock. . . . In terms of the carrier rate in subjects presenting themselves as blood donors, it is arithmetically probable that most plasma pools containing 150 donors are contaminated. It is also probable that 15 to 20% of plasma pools containing 20 to 25 donors each will contain the virus. Hence, small pools of plasma are recommended. The preparation of small pools is a laborious and expensive procedure, necessitated by the frequent sterilization and re-use of equipment. Small pools are also undesirable because such small volumes fail to dilute adequately any abnormally high isoagglutinin titer that may occur in a particular donor. Thus, it is clearly evident that some method must be found whereby blood or plasma may be rendered nonicterogenic without disturbing those qualities in plasma essential in the treatment of shock and malnutrition. . . . The characteristics of virus survival suggest that the serious problem of homologous serum jaundice can be solved in a simple and effective manner that takes into account those principles which govern the viability of viruses and which, at the same time, preserve the stability of the proteins of plasma. Stated more simply, it appears that liquid plasma will withstand room-temperature storage better than will viruses. The thermostability feature of viruses stored in liquid, cell-free state merits clinical and laboratory investigation, for if such storing is successful in eradicating the virus of homologous serum jaundice, plasma could be used as a safe and inexpensive therapeutic agent. —From an Editorial by J. Garrott Allen, M.D., in *A. M. A. Archives of Surgery*, January, 1952.

ROENTGENOLOGIC CONTROL OF NERVE BLOCKS

USE OF IODOPYRACET INJECTION (DIODRAST®)

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and

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The frustrations attendant on lumbar puncture and even venipuncture attest to the blindness of all procedures involving use of needles. This inherent inaccuracy must obviously be greater when needles are directed toward targets that lie relatively deep in body tissues. It is rational, therefore, to expect that needles so directed may occasionally, even in expert hands, be wide of the mark; roentgenologic examination of needle-point position has proven this to be the case.

Clinical regional anesthesia permits the use of relatively large volumes of anesthetic solutions supplemented by narcotics or other depressant drugs. In nerve blocks for pain, particularly diagnostic blocks, such adjuvants are usually prohibited and the criteria of success are entirely different. To some extent, pinpoint accuracy is much more necessary. Moreover, in all blocks for pain the physician is dealing with inscrutable psychological phenomena in which the modifying factors are not only limitless but immeasurable. In doing such blocks, therefore, it is necessary to utilize all possible adjuvants that will establish objectively the accuracy of the procedure.

Since October, 1946, 1,680 patients with pain problems have been treated by one or more nerve blocks in this hospital by members of the anesthesiology department. Beginning in November, 1946, the accuracy of the needle position in 1,124 of these patients was identified roentgenologically. The value of this method has been confirmed in other clinics.¹ It was thought initially that fluoroscopic identification of needle-point position might be satisfactory, but this method was abandoned because it was found to be impractical. The use of stereoscopic films in such procedures as paravertebral thoracic somatic blocks in cases of neoplasm involving thoracic and contiguous soft tissues has been especially valuable.

It soon became evident, however, that determination of needle-point position alone was not sufficient, and, in July, 1947, an attempt was made to utilize contrast media in gathering information relevant to the accuracy of the blocks. A 35% aqueous solution of iodopyracet (diodrast®) was selected as the most satisfactory of contrast media because its physical characteristics were reasonably similar to those of the anesthetic solutions ordinarily employed for diagnostic procedures and to those of alcohol or phenol subsequently used for definitive therapeutic blocks. It was discovered that by such means the area of distribution of the injected solutions might be visualized. Since 1947, a total of 710 patients have received iodopyracet injection as a part of the identification procedure during nerve block therapy.

In the initial 200 cases, preliminary screening tests were carried out for sensitivity to iodopyracet. In no case was it deemed necessary to modify the intended procedure. Although there is a recognized hazard in the use of this contrast agent for intravascular visualization studies, Pendergrass and associates reported only one

fatality in 40,000 cases even in such circumstances.² In the series of cases reported here there have been no instances of untoward reaction attributable to the drug. For these reasons preliminary screening has been abandoned as unnecessary and impractical except in patients with histories of other drug sensitivity or allergic diatheses.

Iodopyracet injection has been used to visualize the distribution of the injected solutions in blocks of the various cranial nerves; blocks of the cervical plexus, the brachial plexus, the cervicothoracic sympathetic chain, and the stellate ganglions; splanchnic and lumbar sympha-

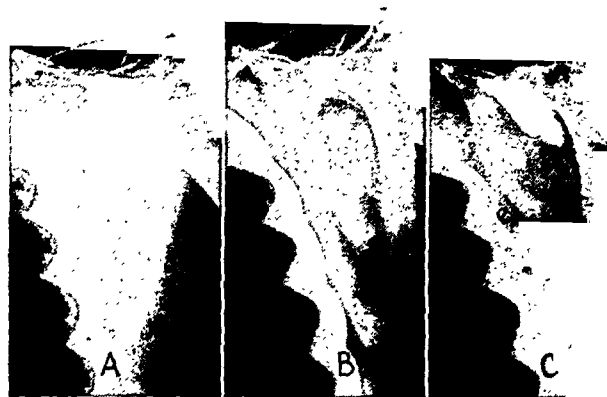


Fig. 1.—Needle position and iodopyracet shadow in a typical supra-scapular nerve block. A, needle incorrectly placed with point in supraspinatus fossa. If injection is made in this position, only a few branches of the supra-scapular nerve will be anesthetized. B, needle correctly placed in the supra-scapular notch. The point can be seen a few millimeters anterior to the anterior surface of the scapula. C, the shadow of 4 cc. of iodopyracet injected through the needle in position in B. With this characteristic spread of solution, the nerve is consistently anesthetized.

thetic block; paravertebral thoracic and lumbar somatic blocks; caudal epidural blocks; and supra-scapular and various other peripheral nerve blocks. It is of no value in cranial nerve blocks, though needle-point position identification by roentgenograms is established routinely in these procedures.³ It is of little value in most peripheral nerve blocks. It is most valuable in blocks of the sympathetic ganglionated chain and the splanchnic nerves, in paravertebral thoracic and lumbar somatic blocks, and

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Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

1. Pender, J. W., and Pugh, D. G.: Diagnostic and Therapeutic Nerve Blocks: Necessity for Roentgenograms, *J. A. M. A.* 146: 798 (June 30) 1951.

2. Pendergrass, E. P.; Chamberlin, G. W.; Godfrey, E. W., and Burdick, E. D.: A Survey of Deaths and Unfavorable Sequelae Following the Administration of Contrast Media, *Am. J. Roentgenol.* 48: 741 (Dec.) 1942.

3. Sweet, W. H.: Trigeminal Injection with Radiographic Control; Technic and Results, *J. A. M. A.* 142: 392 (Feb 11) 1950.

in suprascapular nerve blocks (fig. 1). The iodopyracet injection shadow in figure 1 is typical for a suprascapular block correctly carried out; any other type of shadow indicates maldistribution and an inaccurate suprascapular block.

The needle position and iodopyracet injection shadow in a typical stellate ganglion block are shown in figure 2. It may be seen that, in fact, such a block is a cervicothoracic sympathetic block in this case and that the injected solution is distributed inferiorly as low as the level of the fourth thoracic nerve. This distribution has been confirmed by dissection following injection of iodopyracet.



Fig. 2.—Needle position and iodopyracet shadow in a typical stellate or cervicothoracic block. *A*, needle directed by the anterolateral approach to impinge on the base of the transverse process of the seventh cervical vertebra at the junction with the body. The needle point rests on bone. *B*, the shadow of 12 cc. of iodopyracet injected through the needle in position in *A*. Note that the solution is distributed superiorly to the level of the fourth cervical nerve along the sympathetic chain, envelops the stellate ganglion, and is distributed inferiorly as low as the fourth thoracic nerve. The solution is superior and medial to the dome of the pleura and is actually posterior and medial to the carotid sheath.

cet injection and blue liquid latex.⁴ The discovery that any stellate ganglion block properly executed by any technique inevitably became a cervicothoracic block if more than 12 cc. of solution were injected was a direct result of the use of iodopyracet injection visualization of

solutions in this procedure.⁵ This discovery was a major contribution to knowledge of the technique of cervicothoracic sympathetic block.

In a typical nerve block, such as a splanchnic block for the pain of pancreatitis, the procedure for roentgenologic control is as follows:

The patient is brought to the x-ray theater without premedication, and the needles are placed in position with the patient on the x-ray table. Control films are made with or without stereoscopic exposure to determine needle positions. If the needle positions appear to be inaccurate, the needles are placed again and new roentgenograms are made. When their accuracy is established, the indicated amount of a local anesthetic agent is injected. After 10 to 15 minutes, the patient's pain relief is assessed. If it is satisfactory, an equal volume of iodopyracet is injected and additional films made. After these films are examined, it is possible to determine whether the dye is distributed in the splanchnic area. If such is the case, the appropriate amount of 6% phenol solution or absolute alcohol is injected as a definitive therapeutic procedure. This last injection is not made until at least 15 minutes after the injection of iodopyracet.

SUMMARY AND CONCLUSIONS

The inherent inaccuracy of nerve-blocking procedures may be significantly reduced by using roentgenologic control. In 1,124 cases in which a wide variety of nerve blocks were performed for relief of pain, roentgenograms of needle-point position were of value. In 710 cases, the injection of 35% aqueous solution of iodopyracet (diodrast®) in appropriate amounts was of great value in demonstrating the distribution of the solutions injected for the interruption of pain pathways. Iodopyracet injection appears to be compatible with all the commonly used regional anesthetic solutions and with phenol and alcohol. It is suggested that before phenol, alcohol, or other such agents are injected into the vicinity of all but cranial nerves, a similar amount of iodopyracet should be injected for roentgenologic determination of the distribution of the solution. The use of iodopyracet injections has made possible valuable advances in blocking techniques.

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RESECTION OF A BLIND LOOP SEGMENT OF SMALL INTESTINE

WITH DISAPPEARANCE OF TETANY, HYPOCALCEMIA, AND REFRACTORY ANEMIA

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The purpose of this report is to record the disappearance of tetany, hypocalcemia, and refractory anemia after resection of a blind loop of small intestine showing the pathological features of regional ileitis.

REPORT OF A CASE

M. G., a 34-year-old Italian woman living in the Philippines, was first seen on June 9, 1950, complaining of tetany and severe anemia of two years' duration. The patient had had frequent attacks of generalized abdominal pain and vomiting since childhood. In 1941 acute intestinal obstruction developed, necessitating resection of approximately 2 ft. (61 cm.) of distal ileum involved with regional enteritis. A fistula developed postopera-

tively, and a lateral ileotransverse colostomy without colon resection was done eight months later, followed by resection of multiple fistulas. Fourteen abdominal operations were done by a series of surgeons—Philippine, German, Japanese, and finally American army surgeons—before, during, and after the Japanese invasion. In addition, the patient was treated for shrapnel wounds incurred during the American bombardment. She was then well until 1945, when a completely uneventful subtotal thyroidectomy was done to relieve symptoms suggestive of hyperthyroidism. It is worthy of emphasis that no signs of tetany were noted after this operation and that the patient was in good health until 1948, when persistent fever developed and she lost

22 lb. (10 kg.) but did not have diarrhea. Severe anemia became prominent, requiring 14 transfusions during a two-week period. In early 1949, bloody diarrhea was noted for four days, and persistent anemia was thereafter present, requiring two to three transfusions monthly for a 22-month period. During the past year she received 40 transfusions of 1 pt. (500 cc.) each. Whenever the hemoglobin level fell below 50%, she would become weak, fatigued, and nervous and pass three to four loose stools daily, with normal function being promptly re-established after transfusion. Tetany first developed in 1948, when the level of blood calcium was found to be 6.9 mg. per 100 cc. Subsequent daily intravenous injections of calcium were given to control and treat tetany. Parathormone and moderate amounts of vitamin D were not effective enough to reduce the daily need for intravenous calcium lactate.

She enjoyed breakfast, but within three hours she experienced severe abdominal cramps, distention of the upper part of the abdomen, and anorexia, which prevented eating during the remainder of the day. Hours later, she was aware of reverse peristalsis, which she described accurately as occurring from the site of apparent obstruction until the bolus passed through the more proximal ileotransversostomy, at which time she would experience relief; shortly thereafter she would have a bowel movement.

The patient was emaciated, weighing but 96 lb. (44 kg.) and appeared pale but showed no evidence of vitamin deficiency. Both the Chvostek and Trousseau signs were strongly positive. A well-healed thyroidectomy scar was noted. Multiple scars were noted on the abdomen, which was not particularly tender. The spleen was felt 1 cm. below the costal margin. At the time of the postprandial distress a distended tympanitic mass could be felt in the epigastrium. The results of the remainder of the physical examination, including proctoscopy, were unremarkable except for the occurrence of frank tetany relieved by the intravenous injection of 10 cc. of 10% calcium gluconate.

Results of laboratory examinations were as follows: hemoglobin 9.2 gm., red blood cells 3,450,000, white blood cells 8,200, polymorphonuclear leukocytes 46%, lymphocytes 31%, monocytes 11%, eosinophils 9%, and thrombocytes 200,000. Bone marrow smears were normal. The fragility of the red cells was normal. The result of the Coombs test was negative. Urine specific gravity was 1.018, with 1+ albumin, no sugar, and no red or white cells. No urobilinogen was found in the urine. The initial stool was positive (1+) for blood (guaiac test); some fatty acid crystals were seen, but no ova or parasites were found. Repeat stools were positive (1+ to 4+) for occult blood, and no further fat or fatty acid crystals were found, although undigested meat and vegetable fibers were seen. Repeated searches disclosed no ova or parasites. Stool cultures revealed gamma *Streptococcus*, *Proteus vulgaris*, *Escherichia coli*; no typhoid-dysentery organisms were found. The erythrocyte sedimentation rate was 36 mm. in one hour. Blood serology was normal. Fasting blood sugar was 85 mg. per 100 cc.; urea nitrogen 12 mg. per 100 cc.; carbon dioxide 50 vol. %; chlorides 510 mg., calcium 8.0 mg., and phosphorus 2.6 mg. per 100 cc.; alkaline phosphatase 4.1 Bodansky units; serum albumen 3.4 gm. and serum globulin 2.9 gm. per 100 cc.; and prothrombin time 17 seconds (53% of normal). The basal metabolic rate was +12%. Gastric analysis showed 37 units of total hydrochloric acid after histamine; no free acid was found.

A roentgenogram of the chest and a flat roentgenogram of the abdomen disclosed no abnormalities. Barium enema disclosed an atonic left colon and evidence of an ileotransverse colostomy. Results of gastrointestinal x-ray examinations were confirmatory and revealed a shortened small bowel, due apparently to blockage of the ileum distal to the anastomosis. Transit of barium was rapid, the barium appearing in the colon one hour after ingestion. Despite the rapid transit, the patient had only one bowel movement per day. The patient was prepared for surgery with three transfusions and treatment with vitamin D and antibiotics. The most difficult element of her illness to manage was the persistent hypocalcemia and tetany.

The patient required daily intravenous injections of 10 to 20 ml. of calcium gluconate to control her tetany, despite a high calcium, low phosphorus diet; calcium lactate, 15 gm. per day

given orally in divided dosage; and 10 mg. of dihydrotachysterol given orally daily. Later, as much as a million units of vitamin D (ertron®) intramuscularly was also given. On this regimen her serum calcium ranged from 7.9 to 9.1 mg. per 100 cc.

On June 26, two and one-half weeks after admission, a laparotomy was performed at the Doctors Hospital, New York City. A lateral anastomosis was discovered between the ileum and transverse colon. This was taken down. Distal to this stoma a blind segment of ileum had become distended to form a huge sac, owing to obstruction of the more distal ileum. The collapsed remnant of the terminal ileum, the ileocecal valve, and the right colon were apparently normal. This distended sac of ileum was resected, and end-to-end anastomosis was effected between the proximal and distal ileum. The segment of ileum removed measured 25.5 cm. in length and pathologically showed evidence of chronic, nonspecific ileitis. There was no evidence of demineralization of bones visualized by chest x-ray or in bones seen in



Preoperative gastrointestinal roentgenogram, illustrating sacculation of blind intestinal pouch.

multiple roentgenograms of the abdomen, including good views of the pelvic bones. X-rays of the skull and long bones were not done.

After operation the patient was maintained, once able to take oral medication, on dihydrotachysterol, vitamin D, and calcium gluconate as noted above. Dihydrotachysterol therapy was discontinued on August 4, calcium lactate therapy was discontinued on August 13, and the vitamin injections were discontinued on August 22. Her calcium level fell postoperatively and was 7.5 mg. per 100 cc. on July 22. Thereafter her serum calcium rose to normal levels and remained entirely normal up to the time she was last observed, on September 8. The tetany completely disappeared after July 24. Her stools gradually became negative to the guaiac test, and with ferrous gluconate therapy the hemoglobin rose to 12.0 gm., with a red cell count of 4,260,000 without further transfusions. The spleen no longer was palpable. A repeat gastrointestinal x-ray examination, done on July 10, revealed delayed transit through the small bowel, with a period of about six hours elapsing before barium appeared in the colon. The patient gradually improved and left the hospital on Aug. 18, weighing 124 lb. (56 kg.), a gain of 28 lb. (12.7 kg.) since the date of her operation.

COMMENT

Tetany and hypocalcemia developed in this patient in the absence of diarrhea and despite the administration of parathormone, vitamin D, and calcium. The disappearance of hypocalcemia after resection of 25.5 cm. of diseased small intestine emphasizes the importance of factors other than the length of the small intestine in the development of tetany in patients having regional ileitis. Patients who have as much as 90% of the small bowel resected for mesenteric thrombosis may maintain normal nutritional balance; yet patients with regional enteritis may have severe nutritional deficiency following resection of only 20 to 30% of their small intestines.

Usually in such patients, however, reactivation of the disease in remaining segments of small intestine becomes obvious, and causative factors such as poor absorption due to disease and hypermotility become active and are much more important than any bowel shortening. Active ileitis is often associated with severe constitutional symptoms and may in a yet unknown way affect all functions and processes concerned in maintenance of nutrition.

Still another method of production of tetany in regional enteritis involves the faulty absorption and excretion of fats sometimes encountered in patients with ileitis and universally seen in patients with nontropical

tissue, resulting in hyperfunction sufficient to lower the serum phosphorus level and raise the serum calcium level high enough to prevent tetany. This presumably explains why patients with rickets or osteomalacia have normal serum calcium and no tetany. In this patient tetany developed in part presumably because of inadequate compensatory overactivity of the parathyroids, which may have been functioning maximally since they were unable to respond further to the stimulus of a low serum calcium level.

The patient never had significant diarrhea, nor were the stools ever sprue-like in character. Excessive amounts of neutral fat were not found when the stools were examined with sudan III, nor were fatty acid crystals or soaps seen microscopically. Quantitative fat in stools was not measured. Results of the Sulkowitch test for urinary calcium were repeatedly negative. The transit time of barium through the bowel was increased from one to six hours postoperatively. The lack of evidence of poor absorption due to increased excretion of fats and the absence of diarrhea associates this patient's tetany with vitamin D deficiency. Preoperatively the tetany could be controlled with massive doses of vitamin D and calcium salts. Postoperatively this was no longer necessary, as the patient could absorb and utilize the vitamin D present

Serum Calcium and Phosphorus Levels* in the Case Reported†

Date.....	6/10	6/13	6/17	6/21	6/23	6/27	7/5	7/14	7/19	7/22	8/2	8/11	8/21	9/2	9/8
Serum calcium.....	8.0	8.2	7.4	9.1	8.9	9.7	10.1	9.9	8.1	7.5	10.5	11.6	12.0	9.7	10.7
Serum phosphorus.....	2.6	...	...	...	2.4	...	5.9	3.9	3.3	3.8	3.7	3.2	4.3	3.8	3.2

* In milligrams per 100 ml. † Operation on June 26; vitamin D therapy discontinued August 22.

sprue. Unabsorbed fats combine with calcium in the gut, and both are lost in the feces in the form of calcium soaps. This probably represents a vitamin D deficiency, since it can usually be corrected by large doses of vitamin D and calcium, if the diarrhea can be controlled.

The accompanying table gives the levels of the serum calcium and phosphorus obtained over a three-month period. Large doses of vitamin D (one million units of ertron®) as well as 10 mg. of dihydrotachysterol had to be given to raise the blood calcium to levels above which tetany would not develop. Postoperatively all vitamin D was discontinued when the calcium rose to 12.0 mg. per 100 cc. Thereafter normal calcium metabolism was maintained simply with a normal diet. The low Ca × P product must have favored demineralization of bone, but with a normal alkaline phosphatase level it would appear that demineralization did not occur, at least to the extent of stimulating osteoblastic activity or x-ray evidence of osteomalacia.

Several factors may have contributed to the tetany observed in this patient. Lack of parathormone consequent to the previous thyroidectomy was ruled out by the prompt postoperative recovery and maintenance of calcium metabolism without the addition of vitamin D, calcium, or parathormone to a normal diet. Since the patient had had a thyroidectomy, the parathyroids may have been damaged, but not to the extent of causing clinical hypoparathyroidism; the latter is excluded by the constantly low level of the serum phosphorus. The low serum calcium usually serves to stimulate parathyroid

in an ordinary diet, thus maintaining her calcium metabolism. We are unable to explain why the presence of a blind loop of diseased small bowel (regional ileitis) could cause vitamin D deficiency except by preventing absorption of calcium and vitamin D by the uninvolved small intestine.

The complete obstruction of the ileum well distal to the lateral ileotransversostomy caused a mammoth dilatation of this blind loop, with retention of food for many hours daily. This phenomenon and its influence on intestinal malfunctioning may account for and have contributed to the factors producing the intestinal tetany and, more important, the refractory anemia. The experimental production of such a blind small intestinal loop in dogs has caused intractable anemia.

SUMMARY

The case history of a patient with tetany due to hypocalcemia disappearing after resection of a diseased (regional ileitis) blind loop of small bowel is presented. Preoperatively the tetany could be controlled only with daily massive doses of vitamin D and calcium. The hypocalcemia was not associated with diarrhea or steatorrhea. Postoperatively, with the bowel 25.5 cm. shorter, the patient maintained a normal calcium balance and an excellent state of nutrition. A blind distended loop of small intestine distal to a patent ileocolic anastomosis may have contributed to the failure to absorb calcium as well as to refractory anemia, which required 40 transfusions during the year prior to operation.

RHEUMATOID NODULES OF THE EYE

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In 1930, Van der Hoeve¹ described two cases of a scleral disease that he named scleromalacia perforans. Verhoeff and King,² in 1938, found 14 cases in the literature, added 1 of their own, and discussed them before this section. They gave the first description (with the possible exception of a specimen reported by Hothouse in 1893 and mentioned by Smoleroff³ in his report of three cases) of an eye in this condition that had been removed and studied microscopically.

We have recently studied two cases, clinically and microscopically, that showed some features that emphasize the point that scleral disease, in the rheumatoid state, may give rise to complications that mask the original condition, so that, by the time the patient is seen by the last ophthalmologist to examine him, the origin of the disease may be obscured. Since the advent of cortisone and corticotropin, agents that promise hope of relief, if given before irreversible changes occur, it seems worth while to review the subject again and to call attention to the fact that scleral disease is often a part of the rheumatoid state.

Some years ago, the term "collagen disease" was originated by Klemperer⁴ and his associates to cover a rather ill-defined group, characterized by alterations of a peculiar type in the connective tissue system. Included in this group are rheumatoid arthritis, polyarteritis nodosa, diffuse lupus erythematosus, generalized scleroderma, and dermatomyositis. The common denominator of all these disorders is the tendency to a peculiar type of necrosis that is known as fibrinoid degeneration.

Verhoeff and King² gave this summary of the course of events so well that it cannot be improved on: "An area in the sclera first undergoes simple necrosis. This area soon becomes surrounded by a wall of epithelioid cells. Pus cells then slowly penetrate the wall and surround and infiltrate the necrotic area which has become more or less disintegrated into eosinophilic granules. Ultimately the sequestrum thus formed becomes completely disintegrated and densely infiltrated with pus cells which also become necrotic. That the process of abscess formation is extremely slow is evidenced by the fact that almost no pus cells are to be found outside the wall." The early necrosis in these lesions is fibrinoid degeneration, and this is one of the characteristics that class it as a collagen disease.

Several names have been proposed for this disorder since Van der Hoeve designated it scleromalacia perforans. Rochat called it scleritis necroticans, and Verhoeff and King proposed the term necroscleritis nodosa excavans for the form with cavities, omitting the excavans if cavities had not formed. We feel that rheumatoid nodules of the eye describes the condition.

It is not certain how some deep forms of scleritis fit into the picture, especially the type known as brawny or annular scleritis, and those that are thought to be tuberculous but later are found to be of rheumatoid

arthritic origin. Verhoeff⁵ described a brawny scleritic eye as follows: "Between the tracts of granulation tissue long stretches of sclera, free from cells, have undergone hyaline necrosis, evidently due to sequestration." This, added to the fact that the patient had two scleral nodules and suffered from arthritis, leads one to suspect that brawny scleritis is, in fact, a part of the rheumatoid state. One of us (E. L. G.) treated a young woman for several



Fig. 1.—Rheumatoid nodule from subcutaneous tissue from near hip joint. This is a single nodule cut in step sections demonstrating typical central necrosis and cavitation as is noted in the eye nodules.

years on the assumption that she had tuberculous scleritis and keratitis, because she was sensitive to tuberculin and had recurrent attacks of deep anterior scleritis after the elimination of all known foci of infection.

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Read before the Section on Ophthalmology at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 14, 1951.

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2. Verhoeff, F. H., and King, M. J.: Scleromalacia Perforans: Report of a Case in Which the Eye Was Examined Microscopically, *Arch. Ophth.* 20: 1013 (Dec.) 1938.

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Eventually, rheumatoid nodules developed in the joints of her hands and she had arthritis in her knees, with a recurrence of scleritis. The nodules, joint pains, and scleritis disappeared during cortisone therapy but recurred after it was discontinued. A second course pro-



Fig. 2 (case 2).—Gross nodule in anterior sclera extending into cornea. Central necrosis (fig. 1) leads to perforation of sclera and collapse of globe.

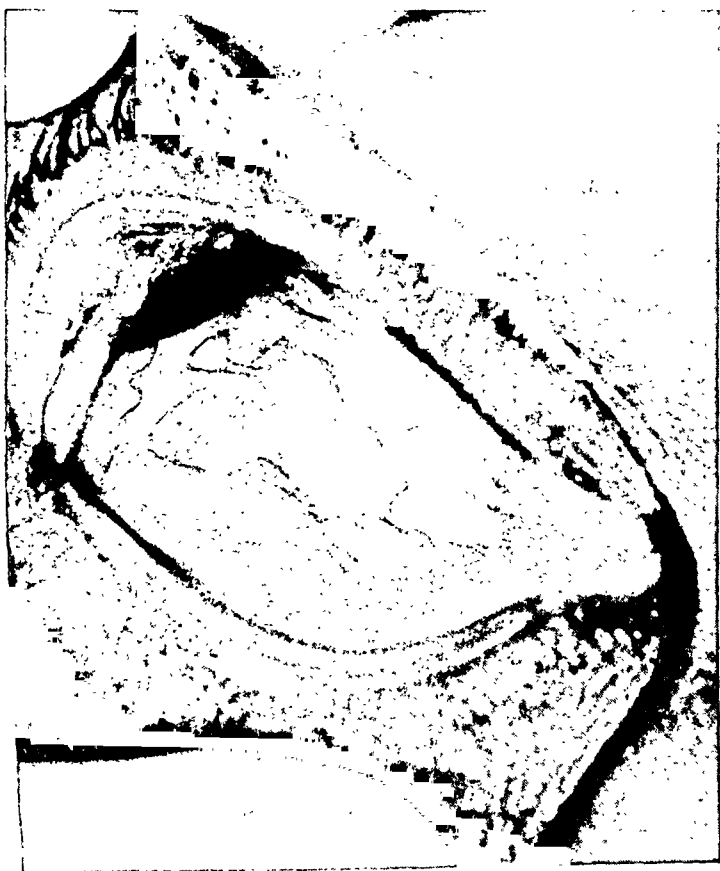


Fig. 3 (case 2).—The gross nodule is seen on the nasal aspect posterior to the limbus. The cornea is turned superiorly and temporally. The episcleral vessels coursing over the nodule are hyperemic.

The association between scleral disease and rheumatoid arthritis has been known since the condition was first observed by Van der Hoeve. Verhoeff and King found it in 10 of the 14 cases recorded and also in their cases. In one case reported by Eggers⁶ and three reported by Smoleroff,³ scleral disease and arthritis were coexistent, and it can be concluded that this is one syndrome.

Many years ago, the term rheumatic iritis was common, but, in recent years, the textbooks have given it little attention. When the focal infection theory came into prominence, some 40 years ago, the rheumatoid state was no longer prominently considered, and focal infection took the center of the stage. It was considered then that nongranulomatous uveitis was largely due to some organism, especially the *Streptococcus*, and that any coexistent arthritis was caused by the same agent. Later, it was suspected that the organisms, instead of



Fig. 4 (case 1).—Marked inflammatory changes in anterior sclera exhibiting central necrosis surrounded by granulation tissue; $\times 23$ (hematoxylin and eosin stain).

invading the diseased spots, acted as allergens to sensitive areas. These theories may be true; they have certainly not been disproved; however, the fact that uveitis, scleritis, and polyarthritis are frequently associated is illustrated by the case of a young man who entered the Veteran's Hospital at Houston with polyarthritis of several months' duration. His eyes were normal when he was admitted for the relief of painful joints. His condition improved remarkably with corticotropin and cortisone therapy, but, because of the scarcity of these hormones, he did not have a complete course. He returned a few months later, with a recurrence of painful joints, severe plastic iridocyclitis, and a definite scleral nodule above the upper limbus. His eye was not affected by cortisone drops or by other therapy but improved dramatically after cortisone injections.

It has been repeatedly stated that scleromalacia perforans is degenerative, first, and that the inflammatory reaction is secondary. If we are to class all severe eye diseases that occur with the rheumatoid state into one group

duced the same results, but later she had a mild relapse of scleritis that responded well to cortisone drops. She still has one small nodule in her hand, but it is not painful.

6. Eggers, H: *Neuroscleritis Nodosa Associated with Chronic Rheumatoid Polyarthritis*: Report of a Case, *Arch. Ophth.* 23: 501 (March) 1940.

and call it rheumatoid disease of the eye, this view would need some modification, because there is no evidence that severe anterior uveitis and, sometimes, sclerokeratitis is primarily other than inflammatory. The following cases call attention to the fact that the primary lesion may be missed unless one is on the alert for it.

REPORT OF CASES

CASE 1.—J. B., aged 65, entered the Veterans Hospital at Houston in June, 1948, for the treatment of arthritis, especially involving his hands and spine. He was readmitted in July, 1949, with a painful right eye. He had been treated elsewhere for an ulcer of the lower part of the cornea of about two weeks' duration. Pneumococci, in smears from the conjunctiva, were found in laboratory tests before admission. In two cultures, only *Pseudomonas* was found by the laboratory. There was a tremendous thickening of the sclera beneath the lower limbus and an ulcer extending upward to the center of the cornea. The scleral nodule



Fig. 5 (case 2).—Macrophotograph of microscopic preparation of anterior scleral rheumatoid nodule demonstrating area of central necrosis. This accounts for the tendency to perforation and collapse of the globe. Note dense lymphocytic collections in episclera extending into cornea; $\times 3$ (hematoxylin and eosin stain).

became necrotic, exposing the ciliary body, and the corneal ulcer became larger and deeper, eventually perforating. Hormones were not available at that time, and no treatment helped him. The eye was enucleated and sent to the Armed Forces Institute of Pathology. According to the laboratory report, the cornea and sclera were partially necrotic and infiltrated by a purulent exudate and there was fibrosis of the limbus. There was an open perforation of the limbus, with coloboma of the iris beneath it and an intraocular hemorrhage, with uveal and retinal detachment. Lymphocytes, plasma cells, and polymorphonuclear leukocytes infiltrated the uveal tract. Cortical lens fibers were degenerated, and the nucleus was pale and homogeneous. The diagnosis was perforating ulcer of the cornea, abscess in the sclera, panophthalmia, intraocular hemorrhage, and cataract of senile type. The pathologist wondered whether this patient had polyarticular arthritis. She regarded this as a rheumatoid nodule of the eye, with secondary infection producing a corneal ulcer with perforation and panophthalmia.

CASE 2.—A. D., a 48-year-old Negro woman, was admitted to Hermann Hospital on Feb. 1, 1950, with the diagnosis of a blind, painful left eye. The eye had become painful in 1939,

when a small nodule developed in the sclera, temporal to the limbus. This apparently perforated, because the pupil became irregular and was drawn toward the temporal side. The nodule was at first red and then became white and firm. A few months later, a small nodule appeared in the lower nasal quadrant. At this time, the patient's joints were painful, and she had fever.

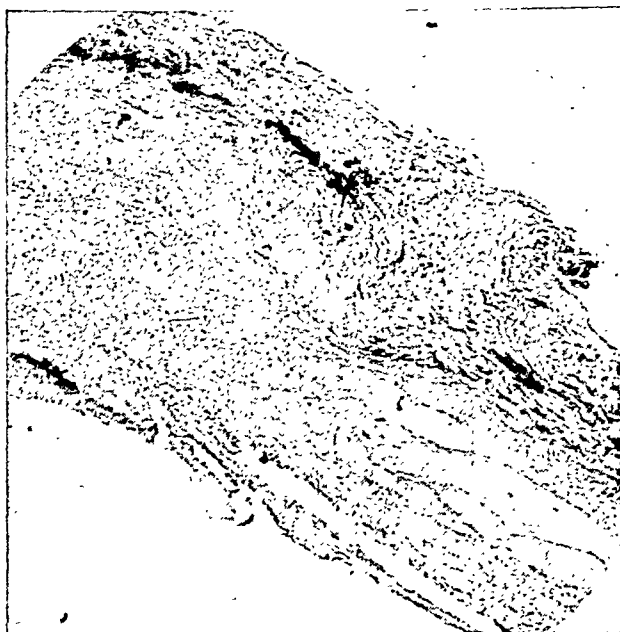


Fig. 6 (case 1).—Inflammatory thickening and central necrosis of sclera of eye; $\times 26$ (hematoxylin and eosin stain).

She gave up her work in a laundry because of weakness. The right eye became similarly involved in 1942, and, within a year, she lost its sight. The vision in the left eye became progressively worse, and she became completely blind in 1944. An interesting sidelight in the history is that before cold or rainy weather, the

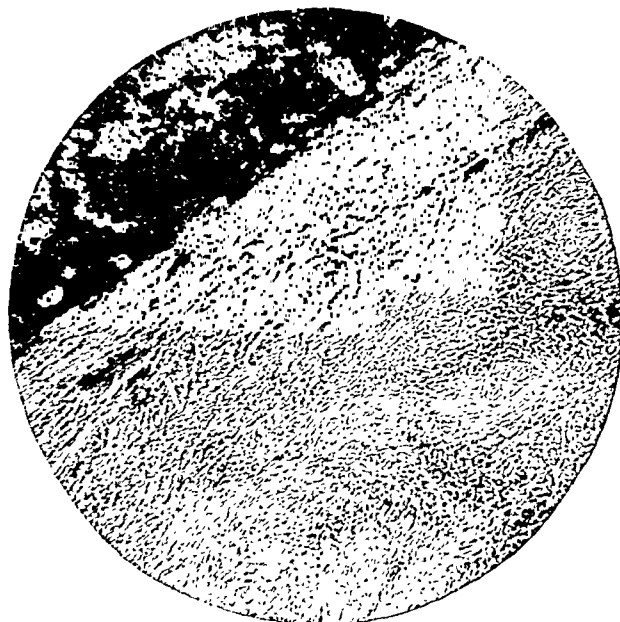


Fig. 7 (case 2).—Dense lymphocytic infiltrate in episclera near rheumatoid nodule; $\times 23$ (hematoxylin and eosin stain).

eyes and joints became more painful. The patient was told by a physician that she had rheumatism and heart disease. The only eye treatment she received was some drops that she used for a short time, with no relief from pain. Within the 12 months preceding admission, the pain in the left eye had become un-

and the patient went to the clinic for relief. The notes on the hospital and clinic records, which are incomplete, state that both eyes were smaller than normal; the left eye was quite hard; the anterior chamber was obliterated; the cornea was opaque, and the eye was congested and painful. Physically, she was the thin, asthenic type, with arteriosclerosis, scoliosis of the thoracic spine, and grade 2 systolic heart murmur. The joints of the extremities were apparently not involved. The laboratory examination revealed nothing pertinent to her condition. The eye was examined in the laboratory of ophthalmic pathology of Baylor University College of Medicine, after which the following facts were reported.

Gross Description.—The specimen consisted of an eye measuring 23 by 24 by 23 mm. The eye was very firm, and the sclera near the limbus, superiorly, was depressed and scarred in two areas. The corneal epithelium was denuded in two large areas. The cornea was opaque and contained many milky white streaks, and there was a scleral scar in the superior temporal quadrant. The sclera was greatly thickened along the equator and along the inferior half. At this point, it measured 6 mm. in thickness, and was white and very firm. The retina was completely detached, superiorly, and partially detached in the inferior hemisphere. No lens was identified. There was a yellow-green translucent exudate beneath the retina and in the vitreous cavity. There were several areas of hemorrhage beneath the choroid, inferiorly.

Microscopic Findings.—On the nasal side, the anterior sclera was greatly thickened and formed a nodule that extended from the equator to the cornea, just past the limbus. This granulomatous nodule contained many foci of necrosis and necrobiosis, surrounded, in part, by epithelioid cells, some of which were palisaded. Foci, rich in lymphocytes, were scattered throughout this nodule in the intervening scleral fibers and surrounded the epithelioid cells; the episclera was particularly rich in lymphocytes, in areas forming follicle-like structures. Pigment macrophages were found throughout this tissue, and the overlying uvea was destroyed. The entire iris was distorted and plastered onto the posterior surface of the cornea, and no anterior chamber remained. The cornea was depressed and folded,

The transudate was eosinophilic and homogeneous in the center and basophilic at the periphery; lymphocytes and macrophages occurred as floaters throughout. The choroid was deeply pigmented and widely infiltrated with lymphocytes that were most numerous near the nodule. The optic nerve was atrophic, and a few lymphocytes were found in the anterior dura and surrounding the episcleral vessels.



Fig. 9.—Central necrosis in rheumatoid nodule from elbow similar to that in figure 8; $\times 24$ (periodic acid-Schiff's stain).

Neither of the cases reported were diagnosed as part of the rheumatoid state, and both were discovered to be such only by examination of the enucleated eye. This probably means that, although a number of papers have been written on the subject, ophthalmologists in general are not very well informed on the syndrome. Since there are now therapeutic agents that offer hope of relief, if not of actual cure, of these formerly hopeless cases, ophthalmologists must be on the alert to recognize the condition in the early stages and must be aware that the eye signs may appear before the joints are affected.

There are many points in common in the histological pictures of the tissues from the joints and periarticular surfaces and from affected eyes, as shown by the illustrations. This may be briefly stated as heavy lymphocytic infiltration in the villi of the joints and in the episclera, central fibrinoid necrosis of the collagen, with palisading of the epithelioid cells, and an occasional giant cell in the second zone.

SUMMARY

Attention is again directed to the fact that certain types of diseases of the eye are a part of the rheumatoid state. Histologically, the nodules about the joints in rheumatoid arthritis show the same picture, with minor variations, as the nodules from the sclera in scleromalacia perforans. Two cases are reported in which the true nature of the disorder was so obscured by intercurrent disease that it was recognized only by microscopic study. Since there is hope of relief by treatment with adrenal steroids and corticotropin, it is important that the condition be recognized early in its course.

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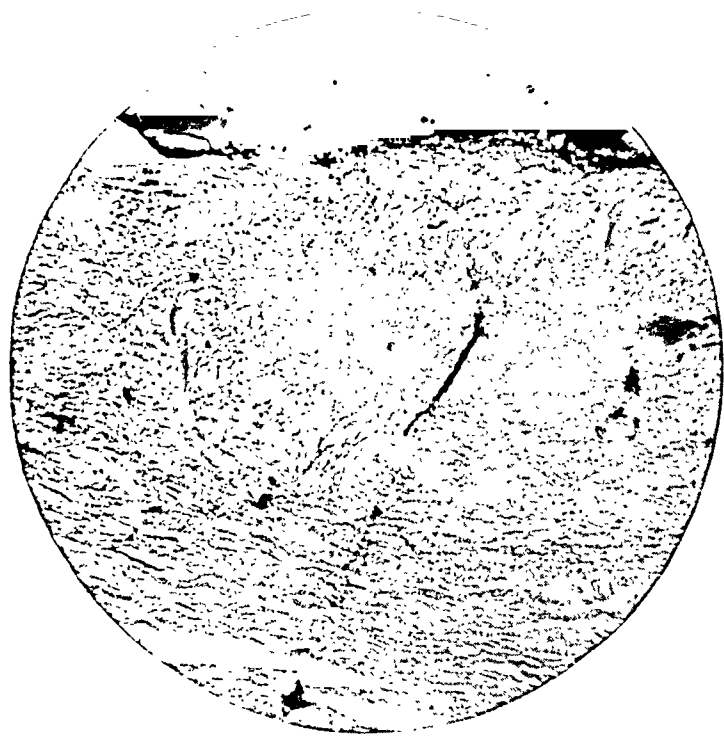


Fig. 8 (case 2).—Scleral necrosis in center of rheumatoid nodule. This stain emphasizes the sharp margins of necrosis surrounded by edematous collagen; $\times 24$ (periodic acid-Schiff's stain).

and the corneoscleral junction was overly vascularized and infiltrated by lymphocytes. Large amounts of transudate filled the subretinal space, detaching the overlying retina, which was thrown into a scarred, distorted, pigmented, funnel-shaped mass that extended anteriorly to the cornea. A few fragments of lens capsule were embedded in the retina and lay between the retina and the nasal side of the iris, which was adherent to the cornea.

ABERRANT PANCREAS: A CAUSE OF DUODENAL SYNDROME

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The anomaly of aberrant pancreas of the duodenum has been inadequately studied and is of sufficient clinical importance to merit more than passing interest. A consideration of this subject was stimulated by our autopsy experience concerning the high incidence of pancreatic tissue observed in the duodenum. There also seems to be a compelling need for the elucidation of the clinical significance of this condition, especially when it involves the duodenum. The accessory pancreas is a common anomalous embryological development, apparently occurring with greater frequency than may be inferred from a survey of the literature. According to the literature its incidence is comparatively low. In recorded studies the incidence varied from 0.04% to 2%. In 1,970 autopsies Duff and co-workers¹ found 21 instances of aberrant pancreatic tissue, an incidence of 1%. In our 410 autopsy studies an unusually high incidence of this condition was observed, especially in the duodenum. In 265 consecutive adult necropsies we found an accessory pancreas in the duodenum in 33 cases, or 12.5%. Among 145 infant necropsies there were 22 cases, an incidence of 15%. Twenty additional cases of aberrant pancreas of the duodenum were found among other adult autopsies, making a total of 75 cases, which will be discussed in this report.

This anomaly is attributable to a faulty embryological development of the pancreas, resulting in the misplacement of pancreatic tissue. The pancreas is developed from the midgut as a budding off from the duodenum in the form of two anlagen. The dorsal anlage is derived from the upper and posterior aspect of the duodenum; the ventral anlage arises from the lower and anterior-medial aspect at the juncture of the duodenum and the common bile duct. It is noteworthy that aberrant pancreatic tissue is most frequently found in the second portion of the duodenum, close to the two embryologic anlagen. Our autopsy study revealed that the duodenum is the commonest site for the development of the accessory pancreas. The embryologic development of the pancreas from the duodenal buds should obviously account for the greater incidence of this anomaly in the duodenum than elsewhere.

In this autopsy study, with the exception of a few instances, the pancreas was found to be normal and of average size and shape. A detailed gross study was made of the aberrant pancreatic tissue, its size, the direction in which the nodule projected, its location within the wall of the duodenum, i. e., submucosal or subserosal, its location in the duodenum, and its relation to the papilla of Vater. The duodenal segment was split wide open, and its walls were carefully examined to determine the presence of an accessory pancreas. Histologic examination was made of each specimen. The aberrant pancreatic growth may be discovered by careful observation and palpation. Although Krieg,² in a review of the literature,

noted that in approximately 60% of cases the accessory pancreatic mass may be discovered by palpation of the bowel wall, this has not been in accord with our experience. In many instances it was difficult to palpate the nodule because of its location in the wall of the duodenum in close proximity to the head of the pancreas. The aberrant nodules appear as firm, irregular elevations or nodules, usually circumscribed and well defined. They may be flat or nodular elevations, the nodular type predominating. The aberrant pancreatic tissue is most commonly situated in the submucosa of the duodenum. The nodule is covered by mucosa and tends to project into the lumen but does not, as a rule, become pedunculated. In rare instances it may be pedunculated and hang into the lumen as a polyp-like growth. The aberrant pancreatic nodule may be mistaken for a neoplasm. Structurally, the nodule is readily recognized as of pancreatic origin in many instances by gross and in all instances by microscope examination. All the structures of the pancreas, such as pancreatic acini, islets of Langerhans, and ducts, are noted in many instances. According to Faust and Mudgett,³ some aberrant pancreatic masses seem to have normally formed ducts that open into the lumen of the bowel.

The growth of the aberrant pancreatic nodules must be extremely slow, since the vast majority are comparatively small in size. Inasmuch as most infant accessory pancreatic nodules measure 1 mm. to 2 mm. in diameter, they apparently tend to become larger with increasing age to adulthood. This may be inferred by the fact that the average size of the aberrant pancreatic nodule in the adult is much larger, as a rule, than that encountered in infants. The accessory pancreas is usually small, varying from 0.1 to 2 cm. or more in diameter. The vast majority are less than 1 cm. in diameter. In only one instance in our 75 cases, the aberrant nodule attained the size of 2 cm. The average diameter in the whole series was 0.57 cm. In 24 of the 75 cases the diameter of the pancreatic nodule measured over 0.5 cm. There have been some instances of unusually large aberrant pancreatic nodules reported in the literature, but these are comparatively rare. Holzwiesler,⁴ reported a case in which the growth measured 6 by 3.5 by 1 cm. In Morris'⁵ case the nodule

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1. Duff, G. L., Foster, H. L., and Bezan, W. W.: Primary Carcinoma of Intra-Ampullary Portion of Duodenum, with Examples of Probable Origin from Aberrant Pancreas. *Trans. Am. Surg. Ass.* 64: 93 (April) 1944.

2. Krieg, R.: On Aberrant Pancreatic Tissue. *Ann. Surg.* 113: 463, 1941.

3. Faust, D. W., and Mudgett, C. S.: Aberrant Pancreas, with Review of Literature and Report of Case. *Ann. Int. Med.* 4: 111, 1930.

4. Holzwiesler, M.: Ein Pankreas divertikel im Duodenum. *Deutsche Wochenschr.* 74: 700, 1917.

5. Morris, J. C.: Aberrant Pancreas in Duodenum. *Am. J. Surg.* 549, 1946.

measured 2 by 1.5 cm. Aside from the natural growth of the nodule, reports in the literature indicate that the accessory pancreas may become enlarged as a result of inflammation or cyst formation or by neoplasm, such as an adenoma or a carcinoma. Multiple accessory pancreatic nodules are observed frequently. In our 75 cases there were 10 with two nodules and one with three nodules.

Aberrant pancreatic tissue may be found in all parts of the gastrointestinal tract. It is most often found in the stomach and duodenum. In our autopsy study of 75 cases involving the duodenum the incidence of an accessory pancreas situated elsewhere in the gastrointestinal tract was negligible. Duff and co-workers¹ found the duodenum involved in 17 of 21 cases, or 81%. Faust and Mudgett,² in 369 collected cases, found 30% and Derbyshire³ 41.7% in the duodenum. The recorded relative incidence of a large collected series of cases according to Feldman⁷ is as follows: stomach 27%, duodenum 26%, and jejunum 20%; the remaining percentage was scattered. Krieg² found aberrant pancreatic tissue in the stomach in 31.5%, duodenum in 31.8%, jejunum in 21.8%, and ileum in 9.4%. In 91 cases, Derbyshire³

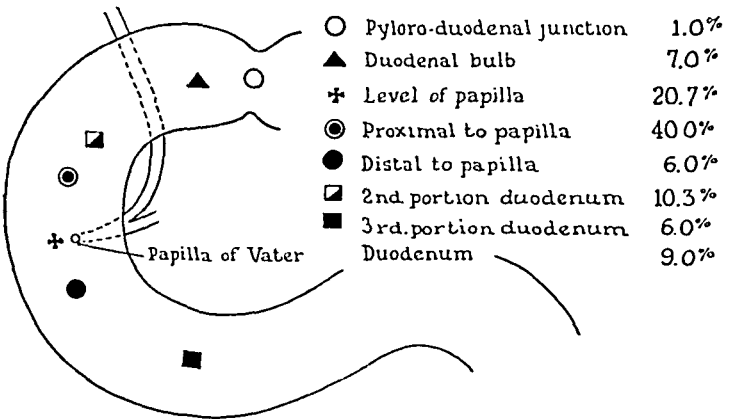


Fig. 1.—Distribution of the accessory pancreas in 75 cases with 87 nodules.

and the accessory pancreas in the stomach in 24.2%, duodenum 41.7%, jejunum 25.2%, ileum 6%, Meckel's diverticulum 2%, and jejunal diverticula 0.9%. Ritter,⁸ in 63 cases, found the stomach involved in 22, or 35%, duodenum in 6, or 9%, jejunum in 25, or 40%, and ileum in 10, or 16%.

Aberrant pancreatic tissue may occur anywhere in the duodenum, but the majority occur within a limited area in the second portion. These are found most often on the mesial and ventral aspects of the duodenum, on the same surface as the papilla of Vater, predominantly between the major and minor papilla, in the area of the embryologic pancreatic anlagen. Accessory pancreatic nodules in over 80% of our cases were found in the second portion of the duodenum, within a few centimeters of the embryologic development of the pancreatic anlagen. The accessory pancreas in the duodenum is charted as to

location in relation to the papilla of Vater and the two anlagen in figure 1.

In our 75 cases with 87 nodules, the nodule was found on the level of the papilla in 18; proximal to the papilla in 35; distal to the papilla in 5; in the duodenal bulb in 6; at the pyloroduodenal junction in 1; in the second part

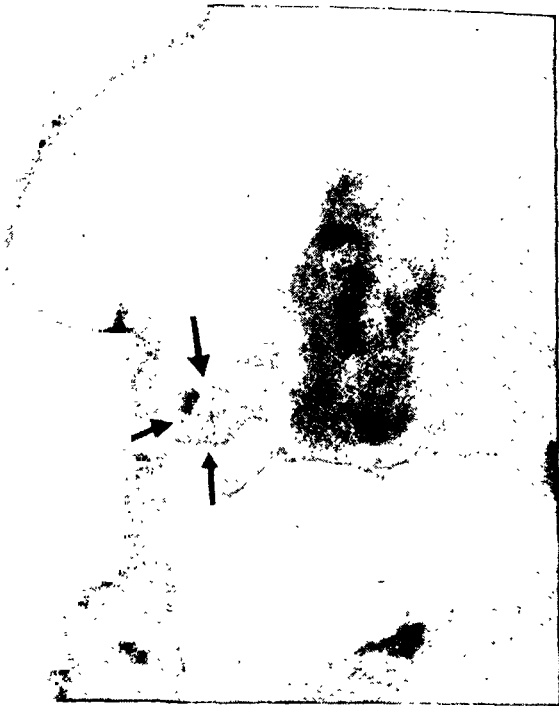


Fig. 2.—Roentgenogram exhibiting a smooth, rounded, polyp-like filling defect in the second portion of the duodenum, characteristic of the larger type of aberrant pancreatic nodules that project into the lumen.

of the duodenum, the exact site not mentioned, in 9; third part of the duodenum in 5; and duodenum, exact site not mentioned, in 8.

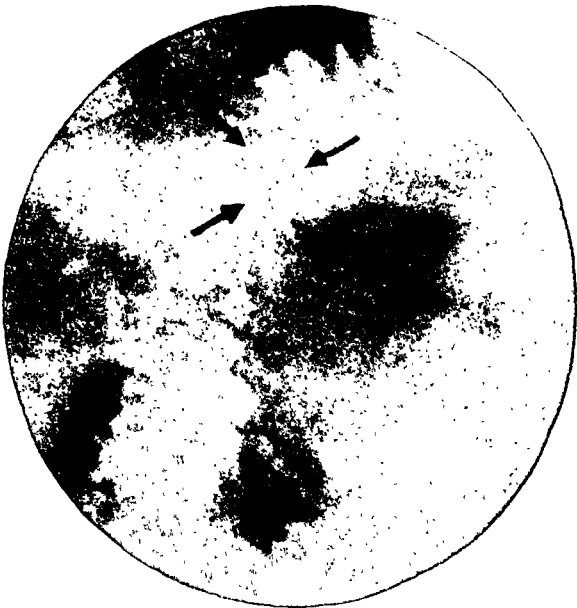


Fig. 3.—An accessory pancreatic nodule in the second portion of the duodenum is shown as a polyp-like filling defect in the mucosal relief view in the spot-film compression roentgenogram.

In these cases the location within the duodenal wall was stated in 76. In 43 the nodule projected into the lumen of the duodenum; in 31 mention was made only that they were directed toward the mucosal surface. In only two instances was the site of the nodule located on the serosal side. In 11 cases no mention was made

6. Derbyshire, R. C.: Studies of Accessory Pancreas, Thesis, Graduate School, University of Minnesota, 1940.
7. Feldman, M.: Roentgenologic Consideration of Normal Mucosa of Duodenum, Radiology 37: 284, 1941; Clinical Roentgenology of the Digestive Tract, ed. 3, Baltimore, The Williams & Wilkins Company, 1948, p. 771.
8. Ritter, L.: Zum klinischen Bilde und Sitz versprengter Pankreaskeime, Beitr. z. klin. Chir. 124: 157, 1921.

of its relation to the wall of the duodenum. The position of the nodule in relation to the duodenal wall was noted to be either submucosal or subserosal. In the majority of cases the nodule was situated in the submucosal tissue and projected into the lumen. With the exception of the two cases in which the nodules were in the serosa, all the nodules were covered with intact mucosa. Barbosa and co-workers⁹ found that 53.8% were located in the submucosa and 23% in the muscular fibers. Delhougne,¹⁰ in 46 cases, found the pancreatic tissue in the submucosa in 45.5%, in the musculature in 25.1%, in the subserosa in 15.1%, and in all layers in 14.2%.

Instances of the association of aberrant pancreas with diverticula of the duodenum have been reported in the literature. Contrary to the belief that this association is common, a duodenal diverticulum was noted in only two instances in our cases. In these, there was no connection between the accessory pancreas and the diverticulum. Inasmuch as duodenal diverticula are common, its relationship to aberrant pancreas must apparently be an incidental finding. Derbyshire⁸ did not find a single instance of diverticulum associated with accessory pancreas in his large series of collected cases. According to Simpson,¹¹ in 17% of 150 collected cases, aberrant nodules were situated in the duodenum and, of these, there were only three reports of an associated duodenal diverticulum. Cave¹² points out that pancreatic tissue may be found at the summit of a diverticulum. Ugelli¹³ reported a case of aberrant pancreas in a duodenal diverticulum. Kalfayan¹⁴ likewise recorded an instance of ectopic pancreas associated with duodenitis and an ampullary diverticulum.

The association with disease or abnormalities of the pancreas is uncommon. The association of aberrant pancreas with an annular pancreas is extremely rare. Chapman and Mossman¹⁵ reported such a case. The association of disease of the pancreas with accessory pancreas has been recorded infrequently in the literature. In almost all of our cases the pancreas was normal. The associated disease of the pancreas is usually an incidental finding that is unrelated to the congenitally misplaced aberrant tissue. However, it is occasionally associated with pancreatic pathology, such as diabetes, inflammation, necrosis, cysts, or neoplasms. In a review of our clinical studies in 43 adult patients, there were four, or 9.3%, with evidence of diabetes. It can definitely be stated that the association of diabetes with an aberrant pancreas is unrelated. We believe that it is merely a coincidental finding.

Complications arising in accessory pancreatic nodules are extremely rare. In none of our 75 cases was there any evidence of complication. However, the following complications may involve the aberrant pancreatic nodule: acute or chronic inflammation, ulceration, adenoma, cyst, and carcinoma. Instances of such complications have been recorded in the literature. Aberrant pancreatic tissue rarely becomes the seat of inflammation. Robson¹⁶ found a case of chronic interstitial pancreatitis involving both the pancreas and an accessory pancreas of the duodenum. Although these do not tend to ulcerate, it is a possibility that must be given consideration. In one of Derbyshire's⁸ cases an ulcer overlay the accessory pancreas of the duodenum. In none of our 75 cases did

the pancreatic nodule directly involve the papilla of Vater, and in no instance was there any evidence of jaundice.

One of the most important conditions to be considered as a complication is the development of an adenoma in an aberrant pancreas. We did not find in our cases any evidence of an adenoma. In 398 collected cases of islet cell tumors of the pancreas, Howard and co-workers¹⁷ found nine instances in which the site of the islet cell tumor was located in ectopic pancreatic tissue; two of these involved the wall of the duodenum. Holman and co-workers¹⁸ reviewed the literature on islet cell adenoma; they found four cases of extrapancreatic tumors and reported an additional case. Of the five, two of the islet cell tumors were found in the duodenum. The accessory pancreas may secondarily produce an obstruction or intussusception of the duodenum, with or without the complication of a neoplasm. Omoda and Kobayasi¹⁹ reported a case of duodenal obstruction and Ross²⁰ a case of intussusception produced by an accessory pancreas. Benjamin²¹ reported a case of a pedunculated pancreatic nodule arising at the duodenojejunal juncture, which was complicated by an ulcerating adenoma and produced an intussusception. Carcinoma is an infrequent complication of aberrant pancreatic tissue. It did not occur in any of our cases; however, occasional cases of this complication are recorded in the literature. Bookman²² and Duff and co-workers¹ each reported a case of carcinoma originating in an accessory pancreas of the duodenum. In 44 cases of carcinoma of the duodenum, Dixon and co-workers²³ found one instance of carcinoma occurring in an aberrant pancreatic nodule.

The age and sex in our group were as follows: of 53 adult patients, 37 were male and 16 were female; of the 22 infants, 12 were male and 10 female. Barbosa and co-workers⁹ found the condition more prevalent in males, with a ratio of 3 to 1. Although in our adult patients the males predominated, in the infants the sex

9. Barbosa, J. J. deC.; Dockerty, M. B., and Waugh, J. M.: Pancreatic Heterotopia: Review of Literature and Report of 41 Authenticated Surgical Cases, of Which 25 Were Clinically Significant, *Surg., Gynec. & Obst.* 82: 527, 1946.

10. Delhougne, F.: Ueber Pankreaskeime im Magen, *Arch. f. klin. Chir.* 129: 116, 1924.

11. Simpson, W. M.: In Stone, W. J.: Medical Contributions to Medical Science, Dedicated to Aldred Scott Warthin, Ann Arbor, Mich., George Wahr, 1927, p. 435.

12. Cave, H. W.: Aberrant Pancreatic Tissue Simulating Duodenal Ulcer, *Am. J. Surg.* 5: 407, 1928.

13. Ugelli, L.: Voluminoso Pancreas accessorio nelle pareti di un diverticolo duodenale, *Policlinico (Sez. Prat.)* 43: 1106, 1936.

14. Kalfayan, B.: Duodenitis with Diverticulum and Ectopic Pancreatic Tissue, *Arch. Path.* 42: 228 (Aug.) 1946.

15. Chapman, J. L., and Mossman, H. W.: Annular Pancreas Accompanied by Aberrant Pancreatic Nodule in Duodenum, *Am. J. Surg.* 60: 286, 1943.

16. Robson, A. W. M.: A Case of Chronic Pancreatitis Probably Starting in an Accessory Pancreas, *Lancet* 2: 1823, 1905.

17. Howard, J. M.; Moss, N. H., and Rhoads, J. E.: Collective Review: Hyperinsulinism and Islet Cell Tumors of Pancreas with 398 Recorded Tumors, *Internat. Abst. Surg. in Surg., Gynec. & Obst.* 90: 417 (May) 1950.

18. Holman, E.; Wood, D. A., and Stockton, A.: Unusual Cases of Hyperinsulinism and Hypoglycemia, *Arch. Surg.* 47: 165 (Aug.) 1943.

19. Omoda, M., and Kobayasi, T.: A Case of Chronic Intestinal Stenosis Arising from the Accessory Pancreas, *Rinsyo Geka (Clinical Surgery)* 2: 37 (Nov.) 1947.

20. Ross, K.: Accessory Pancreas Causing Intussusception, *Australian and New Zealand J. Surg.* 3: 88, 1933.

21. Benjamin, A. E.: Accessory Pancreas with Intussusception, *Ann. Surg.* 67: 293, 1918.

22. Bookman, M. R.: Carcinoma of Duodenum Originating from Aberrant Pancreatic Cells, *Ann. Surg.* 95: 464, 1932.

23. Dixon, C. F.; Lichtman, A. L.; Weber, H. M., and McDonald, J. R.: Malignant Lesions of Duodenum, *Surg., Gynec. & Obst.* 83: 83, 1946.

ratio was almost equal. The condition may be found at any age. The average age of the adults was 60; the infants and children ranged from stillborn to 16 months. Of the 22 infants, 2 were stillborn and 5 newborn; the remaining infants ranged from 2½ hours to 16 months of age. Most of them were less than 2 weeks old.

Frequent casual references to this condition are found in the literature, but its clinical and roentgenologic status have been given little consideration. How often is aberrant pancreatic tissue in the duodenum a causative factor in the production of digestive symptoms? Because of the high incidence of this anomalous condition in the duodenum, it was thought that this investigation might discover a clinical pattern that might be helpful in the diagnosis. From a clinical standpoint it would appear that in the vast majority of cases there is no convincing evidence that the condition is responsible for clinical symptoms. It is possible, however, because of the location of the aberrant pancreatic nodule and its situation within the wall of the duodenum, that any symptoms resulting therefrom may be difficult to interpret. On the other hand, since in most instances the nodule is small in size, it may produce few or no clinical signs. It is noteworthy that at times the condition produces a large intraluminal nodular growth which sooner or later produces digestive symptoms. Although complications are not often encountered, numerous instances are recorded in which the condition was responsible for symptoms.

A review of the clinical records of 43 of the 57 adult cases of aberrant pancreas of the duodenum was made to determine the clinical aspects of this condition. In the majority of the cases there was no clear-cut gastrointestinal symptom complex that could be attributed to the aberrant pancreas of the duodenum. The symptoms were vague and not definitive. Of the 43 cases, 8 (18.6%) presented evidence of gastrointestinal disturbance. In only four instances was a complete gastrointestinal study made, and in these no roentgenologic signs of the accessory pancreas could be detected, because they were too small to be demonstrable. Five of the eight patients were operated on, but the duodenum was not explored. In none of the cases was an aberrant pancreas suspected. Combined roentgenologic and surgical study disclosed 1 case of gastric ulceration, 1 duodenal ulcer, 2 duodenal diverticula, 1 case of intestinal obstruction, 1 carcinoma of the rectosigmoid, 1 case of diverticulosis of the colon, 1 case of ulcerative colitis, 1 case of multiple polypi of the colon with gallstones, and 2 cases of perforating gallbladder. Since there were no complications, the gastrointestinal symptoms were caused by pathologic conditions unrelated to the accessory pancreas. Attention must again be directed to the fact that symptoms produced by an aberrant pancreas are usually the result of some complication. When defini-

tive symptoms occur, there is usually some degree of stenosis of the duodenum, resulting from the enlarged nodule, or it is complicated by inflammation, ulceration, tumor, or an intussusception. Although there are no typical pathognomonic symptoms of this condition, it should be suspected in all instances in which there is an atypical duodenal ulcer history, unaccounted for gastrointestinal bleeding, unaccountable symptoms related to involvement of the papilla of Vater with the association of jaundice, and high intestinal stenosis or obstruction due to tumor development in the aberrant nodule. The symptoms most often simulate peptic ulceration, cholecystitis, carcinoma, or obstruction. When the condition produces symptoms, there may be complaints of abdominal distress, distention, gaseous eructation, nausea, vomiting, diarrhea or constipation, and epigastric pain. The pain, usually caused by spasm, is not characteristic but frequently simulates the ulcer type associated with food ingestion. It has been pointed out that the pain and abdominal distress are often aggravated by ingestion of fried and fatty foods as well as meats. According to Busard and Walters,²⁴ pain may be produced by (1) interference with the passage of food, (2) gastroduodenal retention, (3) peptic ulcer formation from pancreatic enzymes being poured out, and (4) malignant or benign tumor formation. Since the aberrant pancreatic nodule may produce a polyp-like filling defect in the duodenum, it is highly important to establish the diagnosis because the condition may be mistaken for a neoplastic growth. In most of the reported cases, there was an ulcer-like syndrome. Poppi²⁵ reviewed 43 cases and found 39.5% with a clinical diagnosis of gastroduodenal ulceration. In four of the five cases reported by Waugh and Harding²⁶ there were ulcer-like symptoms relieved by food and alkalis. In rare instances the aberrant pancreas may be complicated by an ulceration. Instances of such occurrence have been reported. It may produce bleeding, and cases associated with hemorrhage have likewise been recorded in the literature. Biliary attacks have been reported to occur in some instances. Diarrhea also has been noted in this condition. The physical examination ordinarily yields little information. Rarely is the accessory pancreatic nodule palpable, because most of the nodules are too small to be felt.

Two examples of roentgenologic illustrations of an accessory pancreas were taken from the files of one of us (M. F.). In one of the cases, the nodule in the second portion of the duodenum remained stationary in size for 11 years. The chief gastrointestinal signs in this case were epigastric distress and burning, unrelated to food and without constipation. There seemed to be no clinical relationship between the symptoms and the nodule in the duodenum (fig. 2). In the second case, the filling defect was demonstrated in the relief view in the second portion of the duodenum (fig. 3). In this case there was a clinical history of duodenal ulcer with epigastric pain occurring two to three hours after eating.

According to Norris⁵ and Kjellman,²⁷ the aberrant pancreas has been reported to be a factor in producing hyperinsulinism or hypoglycemia. In none of our cases in which blood sugar tolerance tests were performed was there evidence of hypoglycemia, nor was hypoglycemia noted in Derbyshire's⁶ collected cases. However, one

24. Busard, J. M., and Walters, W.: Heterotopic Pancreatic Tissue: Report of Case Presenting Symptoms of Ulcer and Review of Recent Literature, *Arch. Surg.* 60: 674 (April) 1950.

25. Poppi, A.: Sui pancreas aberranti. (Rivista sintetica completa e contributo coesistito), *Arch. ital. d. mal. d. app. diger.* 44: 534, 1935.

26. Waugh, T. R., and Harding, E. W.: Heterotopic Pancreatic Tissue in Region of Pyloric Orifice: Radiological and Pathological Analysis of 5 Cases of Clinically Suspected Peptic Ulcer in Which Only Pancreatic Rests were Found, *Gastroenterology* 6: 417, 1946.

27. Kjellman, L.: Aberrant Pancreas, *Acta radiol.* 34: 225, 1950.

instance of hypoglycemia was found in which there was an islet cell tumor of the pancreas without involvement of the associated aberrant pancreatic tissue in the duodenum. Of nine patients with islet cell tumors of the accessory pancreas described by Howard and co-workers,¹⁷ eight presented evidence of hyperinsulinism.

In a perusal of the literature, only casual references are noted pertaining to the actual roentgenologic demonstration of the aberrant pancreatic nodule. Since the occurrence of this condition is common and since some aberrant nodular growths attain a large size, it is most probable that many cases are overlooked because of the lack of detailed roentgenologic information and criteria for the diagnosis of this condition. In the roentgenologic examination of the duodenum the transit of barium is rapid, and ordinarily one obtains a relief mucosal picture at some time during the examination. The duodenum is rarely completely filled, because of its rapid emptying. The mucosal view affords a clearer picture of the intraluminal pathologic conditions. Since most aberrant pancreatic nodules to some extent project into the lumen of the duodenum, they should, at least theoretically, produce an intrinsic intraluminal filling defect. Those that occur on the serosal surface are not as a rule visualized; however, when large they produce an extrinsic pressure defect on the contour of the duodenum.

The double contrast method of examination may be utilized to portray more clearly the nodular growth. Air may be introduced into the stomach through a tube or a Seidlitz powder may be given as an aid in the examination. In order to facilitate the passage of air through the pylorus, the patient is placed on the left side for about 15 to 30 minutes before the double contrast roentgenogram is taken. A presumptive roentgenographic diagnosis of aberrant pancreas of the duodenum can be made by demonstration of the polyp-like filling defect. A large number of aberrant pancreatic nodules cannot be demonstrated roentgenologically because of their small size. It should be possible to demonstrate in the roentgenogram those that measure 0.5 cm. and over. However, the flat type of pancreatic nodules would probably not be as easily demonstrable. The diagnosis should be made by repeated examinations and by the process of exclusion. The aberrant pancreatic nodule may produce a filling defect resembling either a polyp or an ulcer. Close observation with spot filming will reveal the mucosal changes, with smoothing out and widening as well as pressure and displacement of the folds. The mucosal folds may be compressed, distorted, flattened, or effaced in the involved area. The polyp-like nodular defect is persistent on the compression spot roentgenograms but may not be demonstrated in some instances when the duodenum is completely filled. When the pancreatic nodule is located in the duodenal bulb, it produces a vacuolated area simulating an ulcer, edema, or a polyp. In most cases of uncomplicated pancreatic nodules, because of their smallness no expansion is shown in the caliber of the duodenum. On the other hand, if the nodulation is as large as has at times been noted in the literature, there may be a localized widening of the lumen of the duodenum. The filling defect produced by the nodule remains stationary in repeated roentgenographic examinations. Roentgenologic examples of the type of filling

defect portrayed by the accessory pancreatic nodule in the duodenum are shown in figures 2 and 3. Aberrant pancreatic nodules occurring in the duodenal bulb are somewhat more difficult to diagnose than those occurring in the second portion. In most of the cases reported, ulceration was considered causative. Guidotti²⁸ reported a case in which a vacuolated filling defect in the bulb was produced. In Littner's²⁹ case the aberrant pancreas produced a polyp-like filling defect in the bulb. In Whiteside's³⁰ case the aberrant pancreas produced a slight elevation of the serous coat of the duodenal bulb, which roentgenologically revealed an ulcer defect. Baylin³¹ reported an instance in which a vacuolated filling defect was demonstrated in the second portion of the duodenum. An important roentgenologic finding, recently pointed out by Kjellman,²⁷ is the demonstration of linear projections, which represent the ducts within the pancreatic nodule. Faust and Mudgett³ have noted that in some instances these ducts open up into the lumen of the duodenum. Thus, when an opaque meal is administered, the ducts become visible. Spasm and irritability of the duodenum resulting from the foreign body effect of the nodule may be noted in some instances. It should be emphasized that, in cases of hyperirritability of the second portion of the duodenum, in the absence of ulceration the possibility of an aberrant pancreas should be considered. The cause of the spasm is explained by Ritter⁸ as being attributable to the attempt of the musculature to abort a foreign body and to chemical irritation of the abnormal composition of the secretion.

In the differential diagnosis consideration must be given to peptic ulcer, polyp, adenoma, cyst, and carcinoma. Although an accurate histologic diagnosis cannot be made roentgenologically, the demonstration of a smooth, rounded, polyp-like filling defect would indicate the presence of a benign growth. Small nodular filling defects in the second portion of the duodenum must not be confused with the normal protrusion produced by the papilla of Vater. It has previously been shown by Feldman⁷ that a small nodular type filling defect may be visible in the mesial aspect of the second portion of the duodenum, which is normally produced by the papilla of Vater.

COMMENT

Since malignant growth in the second portion of the duodenum is comparatively rare, it would seem that the demonstration of a polyp-like filling defect on roentgenograms may be deemed adequate to establish a presumptive diagnosis of aberrant pancreas. The pathogenetic concept in itself is adequate to explain the roentgenologic filling defect. The rarity of malignant growth involving the second portion of the duodenum is most striking. In 275 consecutive autopsies on adults, not a single instance of a neoplasm of the duodenum was found. On the other hand, the incidence of aberrant pancreas in the second portion of the duodenum was notably high. It may therefore be deduced that, when a persistent, nonexpansive,

28. Guidotti, C.: Pancreas accessorio della parete duodenale e sua immagine radiologica, *Arch. radiol.* 15: 34, 1939.

29. Littner, M.: Aberrant Pancreatic Tissue in First Portion of Duodenum, *Radiology* 55: 716, 1950.

30. Whiteside, W. C.: Ectopia Pancreatica Duodenalis, *Canad. M. A. J.* 37: 577, 1937.

31. Baylin, G. J.: Aberrant Pancreatic Tissue as Roentgenologic Problem, *Am. J. Roentgenol.* 53: 277, 1945.

polyp-like nodule is observed in the second portion of the duodenum, this is likely to be the result of an aberrant pancreas. On the basis of pathologic data the roentgenologic diagnosis of aberrant pancreas falls into the realm of possibility. It should be considered in all cases of duodenal disease, notwithstanding the fact that other pathologic conditions may be responsible for the roentgenologic changes.

SUMMARY AND CONCLUSIONS

1. Aberrant pancreas of the duodenum is a common embryologic developmental anomaly, occurring in 13.7% of 410 consecutive autopsies.
2. Over 80% of aberrant pancreatic nodules are found in the duodenum, within a few centimeters of the site of the embryologic development of the two anlagen of the pancreas.
3. Aberrant pancreatic nodules grow slowly but tend to become larger from infancy to adulthood. The nodules are usually small, varying from 0.1 cm. to several centimeters in diameter.
4. Complications are comparatively rare. In our 75 cases not a single instance of complication involving the aberrant pancreas was noted.
5. The majority of patients with accessory pancreas are clinically asymptomatic.
6. A duodenal syndrome occurs as a result of (1) enlargement of the accessory pancreas, producing some de-

gree of stenosis, (2) secondary irritation as a result of a foreign body effect and excessive irritative secretion, producing spasm and hyperirritability of the duodenal segment, (3) ulceration causing either occult bleeding or hemorrhage, (4) the production of some degree of pressure occlusion of the papilla of Vater, as a result of tumor formation, causing biliary symptoms, and (5) complications, such as an adenoma, which produces hyperinsulinism, or other neoplasms, benign or malignant, producing an obstruction or intussusception.

7. It is possible by means of clinical and roentgenologic procedures and by exclusion to make a presumptive diagnosis of aberrant pancreas of the duodenum.

8. Recognition of the presence of an aberrant pancreas is particularly essential, not because of the necessity for surgical removal but because without complications surgery is not indicated. The condition often produces a neoplastic type of filling defect seen in the roentgenologic examination, and the question of surgical exploration becomes a problem, because of the uncertainty of the histologic nature of the nodular growth.

9. Our post-mortem and clinical studies on aberrant pancreas of the duodenum indicate that, when a nodular polyp-like growth is observed in the second portion of the duodenum, without clinical manifestations, the best procedure is to consider surgery only as a last resort and restudy the case at frequent intervals.

747 Lake Dr. (17) (Dr. Feldman).

EFFECTS OF CORTICOTROPIN (ACTH) AND CORTISONE ON DISORDERS OF THE NERVOUS SYSTEM

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The effects of the hyperadrenal state induced by corticotropin (ACTH) and cortisone acetate on various disorders of the nervous system have been studied in 58 patients. The following clinical entities were treated: multiple sclerosis (33 cases), amyotrophic lateral sclerosis (7 cases), progressive muscular dystrophy (3 cases), myotonia dystrophica (3 cases), myasthenia gravis (1 case), Sydenham's chorea (1 case), Wilson's disease (2 cases), Parkinsonism (3 cases), focal myelopathy (2 cases), and epilepsy (3 cases). Some of these

groups contain a sufficient number of patients to enable a significant evaluation; in others, however, only suggestive trends can be noted. Preliminary reports of this investigation have been presented.¹

METHOD OF INVESTIGATION

Corticotropin² was administered intramuscularly every six hours (occasionally every eight hours) in total doses of 80 to 100 mg. per day for courses of five days to two weeks. Frequently, a two week treatment course was repeated. One week periods of saline placebo administration often preceded and followed the corticotropin course. Cortisone acetate was administered at first to several patients intramuscularly in the crystalline suspension, in doses of 200 mg. for one day and 100 mg. per day thereafter, for two to four weeks. During the past six months, it has been given orally, in tablet form, as long-term maintenance therapy, in doses of 75 to 150 mg. per day (in three or four divided doses), after an initial two to four weeks of corticotropin therapy.

All the patients were hospitalized during the period of corticotropin therapy and observed as outpatients during the oral cortisone treatment. During the observation and treatment periods, laboratory studies included determinations of blood electrolytes and sugar, eosinophil

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1. Glaser, G. H., and others: The Influence of Adrenocorticotrophic Hormone (ACTH) on Central Nervous System and Neuromuscular Function, *Tr. Am. Neurol. A.*, 1950, pp. 98-104. Randt, C. T.; Traeger, C. H., and Merritt, H. H.: A Clinical Study of the Effect of ACTH on Chronic Neurologic Disorders in 7 Patients, in Mote, J. R.: *Proceedings of the First Clinical ACTH Conference*, Philadelphia, The Blakiston Company, 1950, pp. 595-602. Glaser, G. H.; Merritt, H. H., and Traeger, C. H.: The Effect of Pituitary Adrenocorticotrophic Hormone (ACTH) on Multiple Sclerosis: A Preliminary Report, in Mote, J. R.: *Proceedings of the Second Clinical ACTH Conference*, Philadelphia, The Blakiston Company, 1951, vol. 2, pp. 141-148.

2. A part of the corticotropin was supplied by the Armour Laboratories and part of the cortisone was supplied by Merck and Company, Inc.

counts, electroencephalograms, electromyograms, and cerebrospinal fluid analyses. Creatin-creatinine excretion was measured in appropriate instances. Quantitative tests of muscle strength were attempted by using a New-man myometer, and motion pictures were taken of certain patients. Special attention was given to fluid balance, salt intake, blood pressure, and weight. Potassium chloride and ammonium chloride were administered to control potassium depletion and fluid retention in certain patients. Criteria of improvement were based primarily on the objective features of the clinical neurological examination. The psychological state of the patient was evaluated in all instances.

RESULTS

Multiple Sclerosis.—Corticotropin and cortisone were administered to 33 patients with multiple sclerosis. There were 23 women and 10 men in the group, ranging in age from 19 to 54 years. The symptoms varied in duration from two weeks (in an episode of optic neuritis) to 14 years. The age and duration distributions are presented in Table 1. There were no significant remissions during the last three year period prior to treatment in cases of more than three years' duration or since onset in the earlier cases. The history of spontaneous oscillations of symptom intensity was carefully noted in all patients. Most of the patients were treated with two 14 day courses of corticotropin and followed for 3 to 18 months thereafter. Ten patients, after an initial corticotropin course, were placed on maintenance oral cortisone therapy for periods of two to six months, up to the present time. The effects were rated with regard to over-all improvement and changes in specific symptom complexes (Table 2). Twenty-one patients (64%) showed either no changes or mild alterations in their over-all status; the alterations were due to either spontaneous oscillation or the psychological suggestion effect of the treatment. However, in five of this otherwise unchanged group, bladder or rectal dysfunction was improved significantly. In two patients, ataxia, particularly of the head and upper extremities, became worse during treatment. These were the only instances of an increase in symptoms (even though relatively slight) in the entire series.

Twelve patients (36%) showed changes suggestive of significant general improvement. The specific symptom complexes most favorably affected (Table 2) were the spastic-paretic, cerebellar or ataxic, bladder, and acute visual (optic neuritis). The effect on spasticity was most pronounced, appearing usually within the first week. The diminution of spasticity allowed a greater utilization of available motor strength, and, thus, strength increased in the involved extremities. These changes occurred without any significant alteration in the status of the deep or pathological reflexes (such as the Babinski reflex) with the exception of an elimination of patellar or ankle clonus in three instances. There were no significant alterations in sensory deficits, although minor fluctuations in intensity and levels of hypalgesia and diminished vibratory sensation were noted. Twenty-one patients had bladder dysfunction, characterized by frequency, urgency, retention, and incontinence. In 13 (60%) of this group, corticotropin induced a moderate

to marked relief of these symptoms within five days (see case report below). Eleven patients had central scotomas of at least six months' duration. In only one patient (with a small scotoma) was any beneficial effect noted. Three patients had large acute progressive scotomas of two weeks' duration. In one case, the scotoma cleared within three to four days. The two other patients showed a moderate, somewhat slower response. Placebo trials could not be utilized because of the nature of the involvement. Oculomotor disturbances (nystagmus, diplopia) were present in 23 patients, and in only one was a significant change noted, a severe third degree nystagmus reverting to a minimal first degree type.

In most instances, all of the effects noted above were transient, appearing only during the course of drug administration and lasting 7 to 14 days afterward. In two cases, the duration of the improvement was six

TABLE 1.—*Ages and Duration of Illness in Thirty-Three Patients with Multiple Sclerosis Treated with Corticotropin and Cortisone*

Age Distribution		Duration of Illness	
Age (Yr.)	No. of Patients	Duration (Yr.)	No. of Patients
19-30.....	9	1	4
30-40.....	11	1-2	10
40-50.....	10	2-4	7
50-54.....	3	4-6	5
		6-10	2
		10+	5

TABLE 2.—*Effects of Corticotropin and Cortisone on Specific Symptom Complexes in Thirty-Three Cases of Multiple Sclerosis*

Symptom Complex	Total No. Patients with Syndrome	Improvement Rating *				
		1-	0	1+	2+	3+
Spastic-paretic.....	28	0	5	10	12	1
Cerebellar.....	21	2	4	11	6	1
Bladder.....	21	0	2	6	9	4
Sensory.....	23	0	20	3	0	0
Visual						
Chronic.....	11	0	10	1	0	0
Acute.....	3	0	0	0	2	1
Ocular movement.....	23	0	10	3	1	0

* 1- = slightly worse, 0 = no change, 1+ = slight improvement, 2+ = moderate improvement, and 3+ = pronounced improvement.

months, without further treatment. There were no notable exacerbations indicative of the development of new lesions during treatment periods. After administration of the drugs was stopped, the course of illness progressed as previously, and, in three instances, this progression was rapid and severe. In no patient did the placebo achieve the same effects as corticotropin or cortisone, particularly in regard to spasticity and bladder dysfunction. The following case report illustrates the type of significant change that can occur coincidental with the administration of corticotropin or cortisone.

REPORT OF A CASE

CASE 26.—A married woman, aged 30, had bilateral visual scotomas for four years and a progressively increasing spastic paraplegia for one year. On admission to the hospital, she was bedridden, had severe, frequent mass reflexes and spasms, loss of sensation below the midthoracic level, and required tidal drainage for bladder dysfunction. The cerebrospinal fluid showed a total protein of 108 mg. per 100 cc., with 10% gamma globulin and no leukocytes. During the first two weeks of corticotropin

therapy, the spasticity and spasms diminished, and the bladder function improved. Substitution of saline placebo injections caused a return of symptoms, particularly of the spasticity. After a second two week course of corticotropin she was ambulatory and did not require tidal drainage. Spontaneous mass movements were absent, and patella and ankle clonus were no longer elicitable. Even the sensory level was less well defined. There was no change in the visual symptoms. The cerebrospinal fluid protein decreased to 56 mg. per 100 cc., with 11% gamma globulin.

During the next six months, while no treatment was given, there was only a slight return of spasticity, and the patient's condition remained improved. Within a week, however, she was again bedridden, with increasing weakness and stiffness of both legs associated with severe extensor spasms. Burning sensations were felt around the trunk, and urinary frequency, urgency, and incontinence developed. The cerebrospinal fluid showed a total protein of 119 mg. per 100 cc., with 15% gamma globulin and 10 leukocytes. Corticotropin was administered again, in doses of 80 mg. per day. Within four days, the spasticity and spasms diminished, and, at the end of two weeks, the patient was am-

TABLE 3.—Cerebrospinal Fluid Protein Changes During Corticotropin Administration in Twenty Patients with Multiple Sclerosis

Case	Before Corticotropin Therapy		On Last Day of Corticotropin Therapy		General Clinical Improvement
	Total Protein (Mg./100 Cc.)	Gamma Globulin (%)	Total Protein (Mg./100 Cc.)	Gamma Globulin (%)	
2	60	24	55	26	Moderate
4	54	13	59	11	Slight
5	55	12	62	12	Slight
6	30	7	33	7	Slight
7	30	14	28	13	None
8	27	9	29	8	Slight
9	34	10	35	8	Slight
10	35	9	53	7	Moderate
11	113	12	86	8	Slight
12	48	10	33	9	None
13	63	24	75	22	None
16	70	10	62	10	None
20	55	10	50	9	Moderate
21	38	20	24	21	Slight
24	120	14	117	16	Slight
26	108	10	56	11	Marked
29	27	13	28	10	Moderate
30	48	10	57	10	Slight
31	64	12	117	9	Marked
32	53	12	45	12	None

bulatory again, with relatively normal bladder function. The cerebrospinal fluid protein decreased to 71 mg. per 100 cc., with 12% gamma globulin, and no leukocytes. She was then given maintenance cortisone therapy (100 mg. per day orally) and was examined biweekly for six months. During this time, her condition remained improved, and she actually showed slow gains in motor function. The cerebrospinal fluid, at the end of this period, showed a total protein of 40 mg. per 100 cc., with 8% gamma globulin. It is felt that corticotropin and cortisone induced and maintained a symptomatic remission. At no time was there any untoward reaction to the drugs. Although the patient had an initial 6 lb. (2.7 kg.) weight gain, her weight remained constant for four months. Her face assumed a slightly moon-shaped appearance, and mild hirsutism developed.

Ten patients were observed while receiving maintenance cortisone therapy. Seven of them had improved significantly with corticotropin therapy, and in six these changes have been maintained thus far during the two to six month period of cortisone administration. One patient regressed to his previous status, even though the cortisone dosage was increased to 200 mg. per day, and 100 mg. per day of corticotropin was given for one week. Three patients, who showed no significant change

with corticotropin therapy, received cortisone for five to six months. During this time, their syndromes remained static.

As indicated by the case described in detail above, alterations in cerebrospinal fluid protein may accompany corticotropin and cortisone administration. This was not paralleled by any significant change in serum proteins, which remained normal in the several cases checked. Complete cerebrospinal fluid analyses were performed prior to and usually on the last day of the second two week course of corticotropin in a representative group of 20 patients (Table 3). Although, in the above case, the clinical changes were paralleled by improvement in the spinal fluid, in general, there was no consistent correlation with either total protein or gamma globulin. The change in Case 31 is of interest; namely, the increase in cerebrospinal fluid protein associated with significant clinical improvement, in contrast to the responses of the patient in Case 26. The significance of these alterations is not clear, particularly since the two patients with the greatest clinical change showed the greatest change in cerebrospinal fluid protein, but in opposite directions.

No patient showed evidence of adrenal cortical insufficiency prior to treatment. All had normal blood eosinophil, electrolyte (sodium, potassium, carbon dioxide combining power, and chlorides), and sugar responses. Generalized asthenia appeared occasionally during both drug administration and immediate withdrawal periods. This condition was not associated with a lowered serum potassium level; however, it occasionally responded to potassium chloride administration. Other deleterious side effects were facial acne and hirsuties and slight water retention, in a few patients. Significant hyperglycemia did not develop in any of this group. The electroencephalograms of 14 of the 24 patients receiving corticotropin showed the presence of diffuse, slightly slow (5-7 per second) activity that had not been present previously. None of the patients receiving cortisone showed significant electroencephalographic changes. Several of the patients showed a slight increase in their usual euphoria, concomitantly with clinical improvement. This reaction was regarded as within normal limits for this setting. One patient had a transient toxic delirium, with paranoid and depressive features, after 26 days of corticotropin therapy, 100 mg. per day. No other significant mental reactions developed in any of the patients in this group.

This investigation indicated that the administration of corticotropin and cortisone or the induction of hyperadrenalism may be accompanied by significant improvement of varying degree in certain symptoms in some cases of multiple sclerosis. The reasons for the response in about one-third of the cases are not clear. The best reactions are seen in patients with symptoms of less than two to three years' duration. These cases are the most difficult to evaluate because of the factor of spontaneous remissions. The therapeutic effectiveness of any agent in this disorder can be regarded as significant only if it (1) induces lasting remissions and prevents relapses, (2) halts further progression, and (3) produces responses in a statistically valid series of cases correlated against the chance factor of spontaneous remission. These condi-

tions are not yet met in this study. The follow-up period and the number of cases, particularly with regard to the patients receiving maintenance cortisone administration, are still inadequate if one considers the variations possible.

The present study has noted effects on existing lesions since improvement in the existing clinical syndrome developed. No definite changes regarded as curative appeared in any patient. There is still only suggestive evidence that relapses may be prevented or actual progression halted by long-term maintenance medication. It is felt that these effects are not true therapeutic changes in the basic disease process; they probably represent secondary physiological phenomena due to the hyperadrenal state.³ There are at least three possible mechanisms that might be considered: (a) an interference with abnormal immunological reactions in the central nervous system, (b) a suppression of inflammatory and connective tissue responses, and (c) chemical changes related to the profound metabolic disturbance (especially in the spheres of potassium, sodium, and carbohydrate metabolism) and their effect on the excita-

after the discontinuation of corticotropin therapy. The course of the illness was not altered in any case.

In general, it was felt that corticotropin was of no therapeutic benefit in amyotrophic lateral sclerosis. The effect on the fasciculations was physiological, only diminishing their intensity and in no instance indicating any alteration in the progress of the illness. The mechanism of this change is possibly related to a diminution in peripheral neuromuscular excitability.

Progressive Muscular Dystrophy.—Corticotropin was administered to two patients and cortisone to one patient with progressive muscular dystrophy. Some pseudohypertrophy was present in all patients. A 23-year-old woman, with a four year history of symptoms, was treated with corticotropin, 100 to 200 mg. per day for 11 days. A 30-year-old woman, with an eight year history, was treated with corticotropin, 80 mg. per day for 28 days. In neither patient were there significant changes in muscle strength. A 6-year-old boy, with a dystrophy of three years' duration, was treated with cortisone (intramuscularly), 50 mg. per day for 18 days and 75 mg. per day for 12 days. There was no change in muscle

TABLE 4.—Analysis of Seven Cases of Amyotrophic Lateral Sclerosis Treated with Corticotropin

Case	Age, Yr.	Sex	Duration of Illness (Mo.)	Dosage, Mg. Per Day	Days of Treatment	Improvement Rating *					Remarks
						Deep Reflexes	Muscle Strength	Atrophy	Fasciculations	Bulbar Symptoms	
31.....	38	M	12	100-300	9	0	0	0	0	—	
32.....	43	M	3	100-200	15	0	1+	0	2+	1+	
36.....	49	F	12	80	28	0	0	0	2+	0	Asthenia developed
37.....	51	F	7	80	28	0	1+	0	—	—	Perforated duodenal ulcer
23.....	76	F	24	40-20	22	0	0	0	0	0	
39.....	50	M	36	80	28	0	0	0	2+	0	
40.....	54	M	12	100	26	0	0	0	2+	1+	Asthenia delirium

* Improvement rating same as in Table 2.

bility of nervous tissue. Investigations of these factors are being carried out at the present time.

Amyotrophic Lateral Sclerosis.—Seven patients with amyotrophic lateral sclerosis were treated with corticotropin (Table 4). There were three women and four men in the group, ranging in age from 38 to 76 years. The duration of illness varied from 3 to 36 months. Muscle strength and bulbar symptoms showed equivocal improvement in two patients. There were no significant changes induced in the deep reflexes. Widespread fasciculations were present in six patients. Within three to four days of corticotropin administration, the fasciculations were diminished in four of these patients by 50 to 75%, both to visual inspection and as experienced by the patient. However, electromyographically, the incidence of spontaneous single unit discharges was not significantly diminished. Within 48 hours after corticotropin therapy was stopped, the visible large fasciculations returned. Generalized muscular asthenia developed toward the termination of therapy in three patients. Significant complications occurred in two patients, a transient toxic delirium with paranoid features (Case 4) and a perforated duodenal ulcer, developing nine hours after the last dose of corticotropin (Case 37,⁴). All of these patients were followed from three to six months

strength. Muscle biopsy performed after the therapy showed histological features similar to those described beforehand: "striated muscle with sarcolemma cell proliferation." Creatin excretion, measured on the last day of drug administration, showed no significant difference from values obtained prior to treatment, the creatin-creatinine ratio remaining essentially unchanged. This finding is similar to that of Shy and associates.⁵

Milhorat⁶ administered corticotropin to two patients with progressive muscular dystrophy of the facioscapulo-humeral type and noted no significant alterations in muscular function. Shy and his associates⁵ treated one patient with a juvenile muscular dystrophy without effect. These investigators also treated four patients with a myopathy of the dystrophic type that appeared in later life, i. e., after the menopause. In three of these patients,

3. Sprague, B. G.: Cortisone and ACTH: A Review of Certain Physiological Effects and Their Clinical Implications, *Am. J. Med.* 10: 567-594, 1951.

4. Habif, D. V.; Hare, C. C., and Glaser, G. H.: Perforated Duodenal Ulcer Associated with Pituitary Adrenocorticotrophic Hormone (ACTH) Therapy, *J. A. M. A.* 144: 996 (Nov. 18) 1950.

5. Shy, G. M.; Brendler, S.; Rabinovitch, R., and McEachern, D.: Effects of Cortisone in Certain Neuromuscular Disorders, *J. A. M. A.* 144: 1353-1358 (Dec. 16) 1950.

6. Milhorat, A. T.: The Effect of ACTH in Myotonia Atrophica and in Progressive Muscular Dystrophy, in Mote, J. R.: Proceedings of the First Clinical ACTH Conference, Philadelphia, The Blakiston Company, 1950, pp. 588-595.

cortisone induced a significant generalized improvement in muscle strength. It seems that corticotropin and cortisone are of no benefit in the usual forms of progressive muscular dystrophy. Further investigation is necessary to clarify the nature and responses of the dystrophy appearing in later life.

Myotonia Atrophica.—Three patients, all men, aged 26, 32, and 41, were treated with corticotropin, 80 to 100 mg. per day for 9 or 10 days. All the patients had the characteristic mechanical and electromyographic myotonic responses, particularly in the hands. Muscle weakness, although present, was not a prominent feature of any case. The mechanical and electromyographic myotonic reactions were not altered significantly in any patient. There were no changes in the general muscular status.

These findings are at variance with those of Shy, who noted an abolition of the myotonic response in two patients within eight or nine days of cortisone therapy. It is doubtful that corticotropin and cortisone would induce different effects on this phenomenon; further investigations are necessary to clarify this problem. Milhorat⁷ reported the effects of corticotropin on two patients with

and eye movements were much improved, and he responded well to a test dose of neostigmine. On the ninth day, a transient delirium with paranoid features developed; this cleared in 12 hours. During the next three weeks, he remained in an improved steady state and was often ambulatory. However, he required neostigmine, 30 to 45 mg. every three to six hours. The tracheotomy was removed. During the following three weeks, a gradual relapse developed, and the patient again became refractory to neostigmine. The patient died from pulmonary complications. He had not been given another course of corticotropin at the time of the relapse.

In this patient, corticotropin apparently induced a transient remission; however, he had been in serious relapse and a state of crisis. This remission might have been a spontaneous occurrence of the type that occasionally follows a myasthenic crisis.

Many patients with myasthenia gravis have been treated with corticotropin and cortisone by various investigators, and it is apparent that a certain variability in response exists.⁷ In general, there was in most patients an increase in the intensity of the myasthenic syndrome during the period of drug administration similar to the asthenia noted above in other neuromuscular disorders. This effect has been reported to be minimized

TABLE 5.—Analysis of Six Cases of Disorders of the Extrapyramidal System Treated with Corticotropin

Case	Diagnosis	Age	Sex	Duration of Illness	Corticotropin Dosage (Mg. Per Day)	Days of Treatment	Clinical Response	Remarks
48	Sydenham's chorea	13	F	1 mo.	80	10	None	No signs of rheumatic activity
49	Wilson's disease	31	F	2 yr.	80	14	None	No changes in liver function were induced
50	Wilson's disease	11	M	7 mo.	80	11	None	
51	Parkinsonism, postencephalitic	59	M	5 yr.	100-200	7	None	
52	Parkinsonism, arteriosclerotic	60	F	1½ yr.	100-200	6	None	
53	Parkinsonism, arteriosclerotic	70	F	4 yr.	40	16	None	Hypertension and hyperglycemia developed

myotonia atrophica. An over-all subjective improvement was noted, but no mention was made of any specific effect on the myotonia. Corticotropin and cortisone seem to be of no therapeutic benefit in myotonia atrophica. Any alterations in the myotonic response should be regarded as due to a physiological change in muscular reactivity by an unknown mechanism.

Myasthenia Gravis.—One patient with myasthenia gravis was treated with corticotropin in this present series.

REPORT OF A CASE

CASE 47.—A 57-year-old man had a four month history of a progressive generalized myasthenia, finally requiring hospitalization, a respirator, and tracheotomy. In the following month, there was little change. He could be out of the respirator for only one or two hours on infrequent occasions and was refractory to neostigmine (prostigmine[®]) bromide. Corticotropin was then administered, 100 mg. per day for nine days; no neostigmine was given during this time. A general improvement was noted within two to three days. After seven days, the patient was able to stay out of the respirator for 12 to 14 hours daily. Speech, swallowing,

by the administration of potassium chloride^{7b}; however, in one case, an increase in "bulbar" symptoms resulted in death on the third day of corticotropin administration.^{7b} Torda and Wolff^{7b} reported significant partial remissions induced by corticotropin in 10 of 15 patients, the improvement usually appearing after the increase in symptoms during the course of treatment. Soffer and co-workers^{7c} noted clinical improvement in one patient that was associated with shrinkage of a thymic tumor following corticotropin therapy. Millikan and Eaton^{7d} described significant but transient improvement in two of five patients treated with corticotropin and cortisone. In most improved patients, neostigmine was still necessary, but the requirement was lowered. The mechanism of action and the therapeutic value of corticotropin and cortisone in myasthenia gravis are still uncertain and require more study.

Disorders of the Extrapyramidal System.—Six patients with dyskinetic syndromes referable primarily to extrapyramidal system disease were treated with a course of corticotropin (Table 5). This group included Wilson's disease (hepatolenticular degeneration), Parkinsonism, and Sydenham's chorea. There was no significant effect on the dyskinesia or on the course of the illness in any patient. The rigidity present in the three cases of Parkinsonism was not affected.

7. (a) Shy.² (b) Torda, C., and Wolff, H. G.: The Effects of Administration of ACTH on Patients with Myasthenia Gravis, in Mote, J. R.: Proceedings of the Second Clinical ACTH Conference, Philadelphia, The Blakiston Company, 1951, vol. 2, pp. 126-140. (c) Soffer, L. J., and others: The Effects of Anterior Pituitary Adrenocorticotrophic Hormone (ACTH) in Myasthenia Gravis with Tumor of the Thymus, J. Mount Sinai Hosp. 15: 73-82, 1948. (d) Millikan, C. H., and Eaton, L. M.: Clinical Evaluation of ACTH and Cortisone in Myasthenia Gravis, Neurology 1: 145-152, 1951.

Corticotropin is probably of no therapeutic benefit in acute and chronic disorders of the extrapyramidal system. No favorable responses were noted in two previous patients with Sydenham's chorea treated with corticotropin and cortisone (Aronson and co-workers⁸). Neither patient with Wilson's disease had any gross alteration in liver function during the period of corticotropin administration. The effects of corticotropin on chronic liver disease have been reported by Bongiovanni and Eisenmenger.⁹ Only transient, variable metabolic changes occurred.

Chronic Focal Myelopathy of Undetermined Origin.

—Two patients in this category have been treated. In both, spinal cord neoplasm had been ruled out by appropriate tests.

REPORT OF CASES

CASE 54.—In a 34-year-old woman a flaccid paraplegia, with a sensory level at T9+10, developed five years previously. Her status had been relatively stationary since that time. Corticotropin 80 to 100 mg. per day, was administered in two 14 day courses. There were no significant changes in her motor or sensory status.

CASE 55.—A 42-year-old man had numbness of the left lower extremity, progressive weakness, and stiffness of the right leg, with involuntary extensor spasms and urinary urgency, over a

the last two weeks of cortisone and for at least two weeks thereafter, two per second more typical spike and wave activity occurred in frequent spontaneous bursts, prior to and during hyperventilation. This could not be correlated with alterations in plasma electrolytes.

Changes of this type and the appearance of abnormal, slow activity in previously normal electroencephalograms¹⁰ indicate an influence of corticotropin and cortisone on the electrical activity of the brain. Further evidence concerning the effects of these substances on cerebral excitability is obtained from reports of convulsions appearing during corticotropin and cortisone therapy in patients without a previous history of seizures.¹¹ The patients had acute disseminated lupus erythematosus, dermatomyositis, acute rheumatic fever, and psychotic depression. These observations are in some contrast to those of Klein and Livingston,¹² who noted an improvement in the seizure incidence and electroencephalograms of four of six children with epilepsy treated with corticotropin. Woodbury and co-workers¹³ found that desoxycorticosterone acetate raises the electric shock seizure threshold in rats. Corticotropin alone depressed then raised the shock threshold, and cortisone alone lowered the threshold and heightened the sus-

TABLE 6.—*Effects of Corticotropin and Cortisone in Three Patients with Epilepsy*

Case	Type of Seizure	Age	Sex	Basic EEG Abnormality	Drug Dosage and Duration	Effects	
						EEG	Seizures
56.....	Focal motor and psychomotor	41	M	Generalized 5-7/sec., right motor focus, synchronous 2-3/sec. with hyperventilation	Cortisone 50 mg./day for 4 days, 100 mg./day for 10 days	No change	No significant change; possible increase in frequency
57.....	Grand mal, petit mal, psychomotor	32	F	Generalized 6-7/sec. Atypical 2-3/sec. spike-and-wave with hyperventilation	Cortisone 100 mg./day for one month	Changed to continuous 2/sec. spike-and-wave activity before hyperventilation	No change
58.....	Grand mal, petit mal	11	F	Continuous 2/sec. spike-and-wave activity	Corticotropin 80 mg./day for 7 days	No change	No change

period of four years. Examination revealed a Brown-Séquard syndrome, with a sensory level at T9 on the left and a spastic weakness of the right leg, with ankle clonus and positive Babinski sign. Corticotropin, 80 mg. per day, was administered for 14 days. During this time, the spasticity almost disappeared, strength improved moderately, the ankle clonus disappeared, and the bladder function became normal. This improvement has been maintained with cortisone 100 mg. per day, over a period of three months. When 50 mg. of cortisone per day is given, there is some return of spasticity.

These findings tend to parallel the observations in the patients with multiple sclerosis, i. e., diminution in spasticity, with better utilization of available strength, but no effect on flaccid paralysis and no significant alteration in sensory deficits.

Epilepsy.—Preliminary studies have been made of the effect of corticotropin and cortisone on the convulsive state. Thus far, three patients with epilepsy have been given these drugs (Table 6). There were no significant alterations in seizure pattern, frequency, or intensity. The electroencephalogram of one patient (Case 57) became more abnormal during the administration of cortisone. Several pre-cortisone records, including some taken during periods of anticonvulsant drug dosage manipulation, showed an infrequent atypical spike and wave activity only during hyperventilation. During

ceptibility to these seizures. Corticotropin, adrenal cortical extract (ACE), and cortisone reduced the raised level of excitability produced by desoxycorticosterone to normal. The mechanism of these changes is still obscure but may be related to intracellular and extracellu-

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lar shifts in electrolytes (particularly sodium and potassium). These factors have been discussed previously.¹⁰ Recently, Ransohoff and associates¹⁴ demonstrated, in one patient, the reversibility by administration of potassium, of coincident electroencephalographic change and toxic delirium induced by corticotropin.

SUMMARY AND CONCLUSIONS

The effects of the hyperadrenal state induced by corticotropin and cortisone were studied in 58 patients with disorders of the nervous system. It was observed that many of the clinical manifestations and metabolic alterations associated with Cushing's syndrome developed in this group of patients. The deleterious effects included weight gain, water retention, hypertension (with corticotropin only), hyperglycemia, rounding of the facies, facial hirsutism, acne, and generalized asthenia. In all instances, these effects could be controlled. Transient toxic delirium occurred in three patients (5%). A perforation of a duodenal ulcer (without preexisting history) developed after corticotropin withdrawal, in one patient.

No significant alterations were noted in patients with progressive muscular dystrophy, myotonia atrophica, Parkinsonism, Wilson's disease (hepatolenticular degeneration), and Sydenham's chorea. Patients with amyotrophic lateral sclerosis showed no improvement in muscle strength, and there was no effect on the progression of the illness. Gross fasciculations were moderately diminished during the period of corticotropin administration. The response in myasthenia gravis cannot be evaluated on the basis of the one case in this series. In

general, the effects of corticotropin and cortisone in this disorder are regarded as variable and equivocal at the present time. A significant increase was noted in the electroencephalographic abnormality of an epileptic patient during cortisone administration. This finding is discussed in relation to induced seizures and other effects on cerebral excitability by these agents.

Approximately one-third of a series of 33 patients with multiple sclerosis showed significant improvement of existing symptoms and signs, primarily of spasticity, ataxia, and bladder dysfunction. Sensory and chronic visual deficits were not affected. In most instances, these changes were transient, appearing only during the course of treatment and regressing afterward or during periods of placebo administration. In only two patients did improvements suggest an induced remission. Problems in the evaluation of this response and the possible mechanisms of action of corticotropin and cortisone are discussed. A group of patients with multiple sclerosis were given maintenance cortisone therapy, but it is too early to determine the effect on the exacerbation rate and course of the disease. No definite changes regarded as curative have appeared in any case. It cannot be stated at the present time that corticotropin and cortisone are suitable therapeutic agents in multiple sclerosis. These findings have merely indicated leads for further investigation.

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TREATMENT OF ATOPIC DERMATITIS WITH CORTISONE

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Soon after corticotropin (ACTH) and cortisone became available for clinical investigation, it was noted that they were effective against a wide variety of dermatoses,¹ including the atopic diathesis.² Initial reports of the use of these drugs in atopic dermatitis were enthusiastic and, in general, created the hope that the therapeutic solution of this perplexing problem was at hand. However, as clinical experience accumulated, it was noted that the pattern of response in atopic dermatitis³ is similar to that observed in rheumatoid arthritis,⁴ lupus erythematosus,⁵ and certain other diseases,⁶ in that it is characterized by marked initial improvement, followed by a relapse when therapy is discontinued. The present study was initiated

for the purpose of determining the therapeutic value of cortisone in a group of patients with atopic dermatitis, when given for a prolonged period of time and under conditions permitting detailed observation. In order to avoid diagnostic confusion, we wish to point out that we consider atopic dermatitis to be the dermatological component of the eczema-asthma-hay fever complex. It is considered by some clinicians to be disseminated neurodermatitis.

MATERIAL

Our case material consisted of 24 adults with chronic severe atopic dermatitis in whose cases there was no diagnostic uncertainty. Borderline, aberrant, and mild forms of the disease were excluded from this study. The patients' ages ranged from 19 to 44, the mean being age 27.7. Eighteen were males and six were females. All were white except for one Japanese male. The duration of the dermatitis in these patients varied from one and one-half years to lifetime. Over one-half the patients had an immediate family history of one or more components of the eczema-asthma-hay fever complex. Nineteen of the patients were hospitalized and were permitted to obtain

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The cortisone (cortone[®]) used in this study was supplied by Merck and Company, Inc. The pregnenolone acetate was supplied by Chemical Specialties Company, Inc.

maximum benefit from bed rest prior to initiation of cortisone therapy. The five patients treated on an outpatient basis had previously been under observation and treatment for prolonged periods of time. In all patients the dermatitis was active at the time treatment was instituted. In one patient the atopic dermatitis was associated with actively developing bilateral lenticular cataracts.

Prior to therapy the condition of each patient was carefully evaluated by a considerable number of laboratory studies. Daily complete blood cell counts, total eosinophil counts, urinalyses, and uric acid and creatinine levels were obtained, and the weight and blood pressure of each patient were measured. Electrocardiograms and measurements of blood sodium and potassium levels, urinary 17-ketosteroids, and fasting blood sugar levels were made at less frequent intervals. It was found that this frequent testing gave no information of value in determining the amount of medication necessary for initial control of the dermatitis or the amount required to maintain improvement. Except for twice weekly urinalysis, weekly blood cell counts, and daily weight and blood pressure determinations, the above tests were discontinued and utilized only when a patient's general condition was such that they were indicated.

METHODS OF TREATMENT

Three general methods of administration of cortisone (cortone®) were evaluated: intramuscular, oral, and topical. After initial experimental observations, it was found that an individual daily dose of 200 to 300 mg., administered either orally or intramuscularly, produced the best results. This dose was continued until maximum benefit was obtained. The medication was then discontinued by one of the following methods: (1) complete and sudden discontinuation, (2) gradual reduction of daily dose, (3) increase in time intervals between doses, (4) administration of a terminal course of corticotropin, or (5) substitution of orally administered pregnenolone acetate for cortisone. Topical medication consisted of application three times daily to one arm of an ointment containing 5.5 mg., and later 25 mg., of cortisone per gram of base, with a control ointment being used on the other arm. In a number of patients, treatment was begun with intramuscular administration of cortisone and later was changed to oral administration. In several instances the reverse procedure was used. The outpatients were treated by both methods. All hospitalized patients were discharged to the outpatient department for further observation and treatment as soon as their clinical condition permitted. A number of patients were used as controls; they were given cortisone and placebo medication at alternate intervals. During the administration of cortisone all patients were placed on low salt diets and were given 5 grains (0.32 gm.) of potassium chloride three times daily.

RESULTS

A daily dose of 200 to 300 mg. of cortisone produced a dramatic improvement in all but one of the patients. The pruritus subsided 24 to 48 hours after treatment was begun, resulting in restful sleep and a general feeling of well-being for the patients. Within 2 to 4 days, objective clinical improvement became apparent and reached its maximum in the next 7 to 14 days. By this time, the skin

appeared normal in all areas except those in which cutaneous involvement had been long-standing, namely, the flexural areas of the extremities. Here, a moderate degree of lichenification generally persisted. Concurrently, the patients' appetites improved, and the majority slowly gained weight. One patient did not tolerate cortisone. He was subsequently treated with corticotropin and obtained a complete, although temporary, healing of his dermatitis.

After healing was complete, usually in 10 to 14 days, treatment was discontinued by one of the several methods previously mentioned. All patients in whom cortisone was abruptly terminated began to relapse 24 to 36 hours after the final dose. The first evidence of relapse was pruritus in the formerly involved sites, followed shortly by the appearance of erythema, papules, and excoriations. Within two to seven days the dermatitis had in most cases relapsed to its pre-cortisone level of severity or had become worse. Because of this initial experience, the following methods of termination of treatment were studied in the hope of maintaining the benefits of cortisone: 1. The daily dose of cortisone was decreased gradually over a two week period. When it reached the range of 75 to 100 mg., most of the patients began to relapse, and all relapsed with a dose below 75 mg. 2. A dose of 200 to 300 mg. was given every second day, then three times weekly, and finally twice weekly. With this schedule, mild symptoms developed in most of the patients on the days cortisone was not administered. When an attempt was made to reduce the individual dose below 150 mg., or to discontinue treatment entirely, all patients relapsed; however, this schedule was partially successful, in that the dermatitis could usually be controlled on an outpatient basis with a dose of 150 to 200 mg. three times weekly. 3. Cortisone dosage was tapered off gradually for one week, during which time corticotropin was administered in a maximum dose of 60 mg. daily. At the end of one week, cortisone was discontinued entirely, and, during the following week, corticotropin was gradually decreased and finally discontinued. This regimen was unsuccessful. 4. In a large group of the patients cortisone was gradually discontinued, during which time the patients were given daily doses of 1 to 2 gm. of pregnenolone acetate by mouth. All relapsed as the cortisone was discontinued, and no benefits could be ascribed to the pregnenolone acetate. It is emphasized that this does not represent a true evaluation of pregnenolone therapy in

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atopic dermatitis, since the drug was administered under circumstances in which there was adrenocortical insufficiency produced by the cortisone.

Patients in this series have been under our observation for periods of 2 to 12 months. Many have received three or four subsequent successful treatments with cortisone, and have been subjected to one or more of the various tapering-off schedules. In none has there been any permanent beneficial effect from cortisone treatment, nor has there been any evidence of the development of cortisone resistance, since, following relapse, all patients again responded satisfactorily to 200 to 300 mg. of cortisone daily.

Orally administered doses of 200 to 300 mg. daily proved in most instances to be as effective as the same amount given intramuscularly; however, in lower doses, 25 to 50% more cortisone was required with oral administration than with intramuscular injection to produce the same results. To make this comparison a number of patients were stabilized on 100 to 150 mg. given intramuscularly daily. The treatment was then changed to the same dose given orally, and the majority showed mild relapses; it was necessary to increase the orally administered dose to restore their former freedom from symptoms. It was also noted that the beneficial effects of orally administered cortisone seemed to be of shorter duration, and more frequent administration was necessary.

All the control patients, to whom placebos were given for three to five day intervals, improved while receiving cortisone and relapsed while receiving placebos.

In two of the five patients receiving controlled treatment with topically applied cortisone ointment, a pustular dermatitis developed on the cortisone-treated side within 48 hours, and it was necessary to discontinue treatment. The others received little or no benefit from the cortisone, and this treatment was discontinued after several weeks.

In the patient with actively developing bilateral lenticular cataracts, cortisone, administered intramuscularly over a four week period, resulted in complete healing of the dermatitis but had no apparent influence on the course of the cataracts.

The following side-effects of cortisone therapy were observed in this group of patients: 1. Mild euphoria occurred in all patients during the time they were symptom free. 2. In two patients moon facies developed after two and three weeks of treatment, respectively. The condition was mild and unaccompanied by other symptoms of Cushing's syndrome. 3. In four patients an acneform eruption developed on the chest or face, which disappeared after discontinuation of therapy. In two a pustular dermatitis developed from cortisone ointment. 4. Most of the patients were of an ichthyotic habitus, perspiring very little. Concomitant with improvement in their dermatitis, they noticed a marked increase in perspiration. 5. In two patients hyperpigmentation developed while they were receiving cortisone. One had a diffuse mild hyperpigmentation on the backs of the hands. The other had small macular pigmented lesions, which, on biopsy, were interpreted as lentigines; these disappeared after cortisone was discontinued. 6. One patient showed intolerance to

cortisone. On the second day of treatment he had a temperature of 102 F (39 C), local soreness and tenderness at sites of injection, and an erythematous papular eruption involving the axillary folds and the upper portion of the chest. Cortisone therapy was discontinued and these symptoms rapidly subsided. He had no such reaction to subsequent corticotropin therapy. In this series of patients we did not observe any of the serious effects sometimes encountered during cortisone treatment. This is possibly a reflection of the younger age and good general health of the patients as a group.

COMMENT

Despite the duration and severity of atopic dermatitis in these patients, all except one responded to adequate dosage of cortisone, and this patient responded to corticotropin. The response began within the first day or two, and maximum improvement was reached in 10 to 14 days. To our knowledge, this is the first medication that has had a consistent beneficial influence on the course of the disease. The maintenance of this level of improvement requires continual administration of cortisone. The disease does not seem to become refractory to cortisone. To date, we have seen little evidence that temporary administration of cortisone influences the future course of atopic dermatitis. The other effects of prolonged cortisone therapy will be the limiting factors in determining the usefulness of cortisone in the treatment of this disease. Although our series of patients represents a group of young and otherwise healthy persons, the control of their dermatitis appears to require a larger maintenance dose than that reported for other chronic diseases.⁴ The undesirable effects of prolonged therapy, particularly with high dosage, have not been sufficiently studied, but there is considerable evidence accumulating to indicate that they may be serious. Until these factors are better known, we believe that cortisone treatment of atopic dermatitis should not be extended beyond a period of four to six weeks.

In our experience, the most objectionable feature of cortisone therapy for this disease was the development, in almost all instances, of a depressive reaction coincident with relapse. Since atopic dermatitis is a chronic illness, patients usually are able to establish a mental adjustment to their condition. However, the dramatic objective effect of cortisone was accompanied by an equally dramatic subjective improvement in our patients that upset their previous adjustment and engendered the belief that a cure for their terrible disease had finally been found. Unfortunately, upon cessation of therapy, they were unable to accept the return of their dermatitis and requested or demanded more cortisone, despite our advice to the contrary. In several persons these demands were, in many respects, comparable to those seen in drug addicts.

At the present state of our knowledge of and experience with cortisone in the treatment of atopic dermatitis, we believe that it has a certain limited usefulness, namely, the control of severe exacerbations that have occurred despite the use of all conventional modalities of therapy. Even in these instances, use of the drug should be discontinued as soon as possible. We believe cortisone is contraindicated in mild to moderate cases.

SUMMARY

1. Twenty-four patients with severe atopic dermatitis were treated with cortisone, administered intramuscularly, orally, and topically.
2. Daily doses of 200 to 300 mg. of cortisone, administered either orally or intramuscularly for a period of 10 to 14 days, produced complete healing of the dermatitis in all but one patient, who was intolerant to the drug. This patient responded to subsequent corticotropin therapy.
3. Intramuscular administration was observed to be the most effective method. Oral administration was satisfactory, but slightly higher doses and more frequent administration were required. Topical application of cortisone ointment was ineffective in a small group of patients.
4. All patients relapsed after cortisone treatment was

discontinued, irrespective of the method of terminating treatment. Remissions could be maintained with continuous cortisone therapy.

5. Other effects of cortisone that have been insignificant in this series of patients are euphoria and diaphoresis in all patients, moon facies in two, pigmentation in two, and acneform eruption in four.

6. At present, we believe the use of cortisone in the treatment of atopic dermatitis should be confined to severe cases in which all conventional modalities have failed to arrest the progress of the disease. In these cases the course of therapy should be limited to four to six weeks.

7. We believe cortisone therapy to be contraindicated in mild to moderate cases of atopic dermatitis.

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PROGRESS IN REDUCTION OF NEEDLESS NEONATAL DEATHS

CHALLENGE TO THE HEALTH OFFICER AND THE MEDICAL PROFESSION

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The continued high neonatal mortality rate, especially of premature infants in the early days of life, must be regarded as a national reproach, and health officers must bear their full share of responsibility for these needless deaths. In Chicago during 1951, 75.8% of all infant deaths occurred during the first month; 88.1% of the deaths during the first month occurred during the first week, and 50.1% of the deaths in the first week occurred during the first day. Although only 8.2% of all the births in 1951 were premature, 69.8% of all the neonatal deaths were in premature infants. The neonatal premature mortality rate during 1951 was 171.4 per 1,000 live premature births, compared with the rate of 6.0 per 1,000 live full-term births.

Although individual physicians over the years have aided in decreasing the number of these deaths, their sphere of influence usually has been so limited that each working alone could accomplish relatively little. The health officer of a municipality, however, is well fitted to assume a major share of the joint responsibility for the reduction of the neonatal mortality rate. In failing to do so, he renders a disservice to his community.

It was evident to us as early as 1935 that one important reason for slow progress in reducing infant mortality was lack of knowledge of the exact causes of infant deaths. Many of the reports of causes of infant deaths, as obtained from death certificates everywhere, were inaccurate, misleading, and provided little usable information, because they were not based on satisfactory postmortem examinations and complete clinical investigations. If the problem of decreasing infant deaths was to be properly attacked, reliable information as to the most important causes first had to be obtained. Therefore, an extensive, long-range study of infant mortality, as shown by satisfactory postmortem examinations, was started by us in 1935. (To be considered satisfactory, a

postmortem examination must have been done by a competent pathologist who was familiar with fetal and infant pathology; must have included a gross examination of the entire body, including the brain and cranial cavity; must have included a microscopic examination of any tissues necessary to make an accurate diagnosis; and must have included a complete report of the results of the examination. Whenever the postmortem record stated that microscopic examinations of all important tissues were not made, but the cause of death was obvious to the trained pathologist from the examination made, the examination was also considered satisfactory.)

The health department through its chief health officer initiated, integrated, and implemented this study and was the driving force behind it. The formulation and activation of the study were facilitated by the constant help and cooperation of Chicago's physicians, hospital administrators, nurses, and others. Physicians were assigned to review the course of events preceding the death of every infant. To obtain all possible pertinent information, the attending physician, parent, nurse, and many others were questioned, and hospital records were studied. A real effort was made to have postmortem examinations performed in every case, and within a short time postmortem examinations were being performed on approximately 85% of all dead infants (a percentage that is still in effect). The services of a highly trained pathologist especially interested in the problems of early infancy were obtained. She stimulated pathologists in the city to a

From the Chicago Health Department. A grant from outside sources was not made available to support this work.

President, Chicago Board of Health, Registrar of Vital Statistics for Chicago (Dr. Bundesen); Associate Professor of Pathology, Department of Obstetrics and Gynecology, University of Chicago School of Medicine; Pathologist-in-Chief, Chicago Health Department (Dr. Potter); Epidemiologist, Chicago Health Department (Dr. Fishbein); Biostatistician, and Chief, Public Health Methods, Chicago Health Department (Mr. Bauer); and Director of Nurses, Chicago Health Department (Miss Plotzke).

greater interest in this field and to improvement of post-mortem examinations. Many of the examinations were performed by her or under her supervision.

A staff of workers was assigned to collect data on all clinical investigations and postmortem examinations and to determine how the then available, limited data could best be put to use. Evaluation of the information obtained by our preliminary studies during the formative, developmental years revealed important factors responsible for infant deaths that required investigation as much as the pathological lesions causing death. One of the important examples of the conditions brought to light by these investigations was the unsatisfactory conditions in the maternity divisions of hospitals.

We, therefore, continued to determine the pathological lesions causing death but expanded our study,¹ using a staff of specially trained personnel to explore other cardinal factors. From these studies we became aware that the greatest effort must be concentrated on the neonatal period, particularly the first day or two of life, and on the smaller premature infants. Most deaths in infants in the first days of life and in premature infants were found by us to be directly related to conditions existing in the mother during pregnancy, to the conduct of labor and delivery, and to the immediate postnatal care of the infant, and that is where we had to intensify efforts. In many cases hospital administration was unsatisfactory in assuring the best facilities for the care of mothers and their infants, and all steps were not being taken to make sure that hospital procedures were satisfactory.

From our expanded investigation we obtained much valuable statistical data that aided us in critically but constructively appraising unsatisfactory conditions leading to neonatal deaths, especially in hospitals, for it was there that most of the births and neonatal deaths were occurring. Our study aided us in reevaluating our previous procedures, so that, wherever necessary, new and more effective ones were instituted. As we more fully realized the needs of the program from our preliminary observations, a statistical department was instituted with a large staff of trained workers, under the direction of an outstanding recognized biostatistician, to tabulate and analyze the vast amount of data in our possession.

1. This expanded study was aided by a number of other outstanding obstetricians, pediatricians, and biostatisticians throughout the nation. Among the obstetricians, Fred L. Adair's pioneering work led us to the inauguration of a full scale long-term program of obtaining satisfactory postmortem examinations on a large series of infant deaths. Nicholson J. Eastman has pioneered in the study of high rates of premature births in women of lower socioeconomic status. Howard C. Taylor suggested to us that graphs would increase the value of the presentation and improve the presentation of the material as a teaching medium. Among the pediatricians, Francis F. Schwentker brought to our attention the newer knowledge relating to high humidity for premature infants, and Julius Hess guided us in our study of mortality among premature infants. Among the biostatisticians, Philip Hauser pointed out the close relationship between socioeconomic status and neonatal mortality. Margaret Martin and Paul M. Densen drew our attention to the need for determining mortality rates in order to draw sounder conclusions.

2. The complete presentation of the 22 objectives, combined into 11 sections, is in process of publication and will be available from the Chicago Health Department. It includes all the details of statistical data connected with the problem, and details the many problems encountered in reducing neonatal mortality. It describes completely the plan for solution of the problem and enables those interested to follow the entire procedure upon which our philosophy for controlling neonatal mortality is based. Particular care has been taken to make the descriptions and discussions as detailed and complete as possible for those who have a direct and intensive interest in our activities.

3. Federal Security Agency, Public Health Service: Personal communication to the authors, Feb. 9, 1950.

These unique statistical data were for day-to-day use in guiding us in the control of immediately remediable conditions as well as for long-term studies to direct the general course of action.

PROGRAM TO REDUCE NEONATAL MORTALITY

Altogether the data accumulated by our expanded study gave us the essential information from which we developed a workable, long-term, 22 point program,² with each item covering a well-defined objective. For this paper we have combined these 22 objectives into four all-inclusive major objectives. In outlining our plan of procedure we constantly kept ourselves aware of our objectives, our course of action, the desirability of collecting and analyzing reliable statistical data, and the need for recording and acting upon our resultant conclusions, all in full accord with the views of those men of integrity who are so successfully piloting the course of organized medicine.

OBJECTIVES

Our first major objective was to outline the way in which the health officer with the aid of the medical profession can carry out his part of the program for reducing neonatal mortality. We carefully reviewed the duties and obligations of a conscientious health officer, the requirements of the city ordinances for hospitals, the requirements of the regulations of the board of health for maternity divisions of hospitals, and the facilities available to the health officer. This review showed that the health officer does have a vital role in reducing neonatal mortality. He also has the authority, personnel, equipment, official records, and adequate data to determine many of the factors responsible for neonatal mortality.

Although local health officers are among those most concerned with the problem of neonatal mortality and have so much basic material to aid in its reduction, nevertheless, in the national meetings organized to discuss this problem, the experienced local health officer has seldom been invited to attend. It has been stated, "Some time ago, the Children's Bureau called a meeting of various authorities concerned with the problem of neonatal deaths in order to ascertain what further steps might be taken to work toward a solution. At this meeting were representatives of the Public Health Service, the Children's Bureau, The National Office of Vital Statistics and the American Hospital Association, as well as a number of leading obstetricians and pediatricians."³ It will be noted that local health officers were not mentioned as being present.

Our second major objective was to determine the causes of neonatal deaths and all the factors that might have contributed to them. To find the causes of death we set up methods and techniques of making postmortem examinations and clinical investigations for determining the specific pathological lesions responsible for deaths in a large enough number of cases to be representative. Among other things our investigations were planned to find how conditions in the infant's mother and associated with the infant's birth contributed to neonatal deaths; to study all the causes of death, as shown by postmortem examinations and clinical investigations, and to analyze their percentage distributions; to analyze the essential causes of death when an immediate and underlying cause

were both present; to study the causes of post-neonatal deaths to compare them with the causes of neonatal deaths; to find the age period when neonatal mortality was highest; to determine how the birth weight affected the survival of infants; to calculate the mortality rate for each cause; to study the effect of race; to determine the effect of socioeconomic status; and to prepare statistical tables and graphs to demonstrate more clearly all the important points.

Our third major objective was to determine what faulty hospital and health department procedures were responsible for high neonatal mortality and wherein the hospital and the health department had not seen to it that a number of these faulty procedures were promptly and completely corrected. To accomplish this successfully two appraisal and scoring systems were employed, one for hospitals and one for the health department. Procedures in hospitals were carefully studied and evaluated, since certain faulty hospital procedures as well as certain factors neglected by the health department were responsible for many needless deaths. To help reveal faulty hospital procedures, hospital records had to be made complete and accurate, to depict correctly what occurred prior to the death of every infant.

Our fourth major objective was to formulate and make operative a workable plan for correcting the continuing deficiencies of hospitals, the health department, and others. To construct such a plan, we knew an earnest effort had to be made to discover hospital errors quickly, and set up procedures for promptly correcting and keeping them corrected, as well as for correcting faulty procedures and neglected factors that were contributing to deaths in the home. We also realized our own health department procedures had to be promptly corrected and kept corrected, and we saw the need for assuring that obstetricians, pediatricians, nurses, hospital administrators, nutritionists, and social service agencies had the facilities, personnel, and authority necessary to carry out their part in the program.

COURSE OF ACTION TO ATTAIN OUR FOUR MAJOR OBJECTIVES

To attain our first objective, the health officer formulated regulations in cooperation with the Joint Maternal Welfare Committee of Cook County covering the personnel, procedures, and equipment in hospitals. This committee was organized by the Chicago Health Department, together with local medical societies, in 1937. It was made up of members selected by each of the groups in the city especially concerned with the care of mothers and infants, including the Chicago Medical Society, Chicago Pediatric Society, Chicago Gynecological Society, Chicago Hospital Council, American College of Surgeons, Cook County Coroner's Office, Infant Welfare Society, First District, Illinois State Nurses' Association, and the Chicago Health Department.

The health officer enforced the regulations of the maternal welfare committee. He instituted a program for obtaining satisfactory postmortem examinations and complete clinical investigations on a large enough number of neonatal deaths to be statistically significant. He made a careful study of hospital procedures and errors responsible for neonatal deaths, and took steps to correct

them, and he studied his own procedures and then improved them.

To attain our second objective, we set up a program for obtaining postmortem examinations and clinical investigations on as many infant deaths as possible. Our special pathologist did a large number of examinations, and aided other pathologists in many different hospitals in interpreting their postmortem findings. The qualifications of those performing the postmortem examinations on infants were investigated to determine whether or not such postmortem examinations as they did were satisfactory for our analyses.

Since, by 1950, the personnel and facilities were available, we compiled and thoroughly studied the extensive data on postmortem examinations and clinical investigations collected during the 14 year period, as well as the conditions in hospitals that contributed to neonatal deaths. From 1936 through 1949, satisfactory postmortem examinations were made in 10,021 neonatal deaths. Many more postmortem examinations were performed but were not included in our study because they were incomplete or of poor quality. Only results of satisfactory postmortem examinations were included in our analysis. Results of accurate clinical investigations were obtained and analyzed in 8,905 of the 10,021 deaths.

The causes of death, as determined by postmortem examinations, and the data from the clinical investigations, such as age at death and weight at birth, were coded and classified. Then they were transferred to International Business Machine cards and tabulated by machine. From these cards 624 tables with more than 300,000 cross tabulations were prepared. Only 112 of the tables that showed the more significant and essential data and brought out the most important points in relation to our program for reducing neonatal mortality were selected and included in our complete presentation. The 512 remaining tables that do not reveal facts very pertinent to the purpose of this presentation were available for future study. In addition, 31 graphs were prepared to illustrate the most important points in the tables.

To attain our third objective, we made thorough, complete inspections of the maternity divisions of hospitals, using the all-inclusive hospital inspection, rating, and accounting forms (scoring form) to aid in making these inspections uniform and complete. This audit form has been in successful use for some time, and we believe it is the first such form that has been utilized in making hospital inspections complete and thorough. We have made a careful search of the medical literature and can find nowhere reference to such an all-inclusive, detailed plan of enforcing hospital regulations. Another scoring form was formulated for rating the efficiency not only of health department hospital survey teams but of the health officer as well. Complete and constant enforcement of all our regulations was made possible by the adoption and efficient operation of these two audit and scoring forms. The audit and scoring form for hospitals made it possible quickly to detect hospital errors and violations of the regulations, since it included all items concerning personnel, procedures, facilities and records, and hospital services necessary for the maternity divisions of hospitals, and scored violations of the city ordinances and regulations of the board of health.

Our survey teams of trained physicians and nurses used the appraisal system to detect and record accurately the specific errors and violations in the various hospitals, especially in those that had comparatively high mortality rates in premature or full-term infants. After the hospital was inspected, errors in techniques and procedures, lack of facilities, and deficiencies of personnel could be related to the mortality rate of the institution, so that the direction of effort could be determined.

The audit and scoring form for the health department is used by the health officer to score the efficiency of the survey teams and of the health officer himself. The survey team is charged with the duty of discovering violations of the regulations, unsatisfactory techniques, and other factors contributing to needless neonatal deaths, and of following through and actually obtaining correction of these conditions. The health officer, who is charged with the duty of keeping his personnel working efficiently on the problem, scored himself to make sure that he and they did not permit the regulations to be ignored or breakdowns or violations to slip by unnoticed. Incidentally, to do this job well, the health officer had to be critical of himself as well as of his personnel to make sure that no lapses occurred. He actually scored himself on the degree of fulfillment of his executive functions in this connection, with the same zeal as he scored the hospitals.

Tables of mortality rates of groups of infants of various birth weights in each hospital were prepared, from which the age and weight groups with greatest mortality could be determined. For example, these tables show the mortality rates for premature infants that die during the first day, week, month, and year. They show the mortality rates for premature infants of various weights and for full-term infants. Thus, high mortality rates in full-term infants often mean that deaths are occurring that could be prevented by good obstetric practices, since most deaths in full-term infants during the first few days are due to obstetric causes, including lack of prenatal care. High mortality rates in premature infants (particularly the smaller ones) also often indicate poor obstetric management and inadequate prenatal care, but in addition signify lack of satisfactory early premature infant care, since with optimal care many of even the smallest infants will survive.

The health officer compared the rates in the various hospitals and determined in which hospitals the rates were highest. He also checked the changes in rates for the city as a whole and of each hospital, year-by-year, and month-by-month. When rates were increasing, he determined the cause by investigating the quality of nursing care, obstetric procedures, and facilities, and made every effort to cooperate in obtaining the necessary corrective action.

Studies of the facts pertaining to individual deaths aided in bringing to light certain preventable factors, such as failure to be properly prepared promptly to transfuse an infant with erythroblastosis, because the diagnosis was not made in advance; because blood and transfusion facilities and specially trained personnel were not available in the hospital; or because of failure to diagnose and treat infections efficiently. By making certain that such

deficiencies and many others were corrected as soon as detected, similar occurrences were generally prevented.

To attain our fourth objective, we formulated and made operative a definite workable, detailed plan to reduce infant mortality, now known as the Chicago Plan. In summary, as it is in operation today, the plan includes the thorough investigation of every infant death. Emphasis is placed on the importance of a satisfactory postmortem examination. The clinical history is obtained as soon as possible after death and is correlated with the postmortem findings. The records of the postmortem examination and clinical investigation are collected, and the data from them are carefully analyzed. Data pertaining to live infants, such as those from monthly hospital reports, are collected for special studies to determine mortality rates.

Meetings are held with physicians by the Joint Maternal Welfare Committee of Cook County and its subcommittees to discuss maternal and infant deaths, in order to familiarize physicians with preventable factors and to obtain their full cooperation, since the highest quality of obstetric and pediatric care can be developed only with full cooperation of all concerned. Individual conferences are held by the health officer with hospital administrators, physicians, and others when mortality rates are too high, to talk over and improve existing conditions in hospitals. Home calls are made by nurses to instruct mothers in the care of their infants when no private physician is in attendance. Printed material concerning prenatal care and care of infants is made available and distributed without charge.

Regulations for maternity divisions of hospitals, newborn and premature nurseries have been passed and are now enforced. They include specifications for the location, equipping, and staffing of rooms for labor, delivery, and postpartum care of mothers and nurseries for infants. Hospitals are required to have on duty at all times nurses specially trained in the care of premature infants. The nursery for newborn infants must be under the direction of a well-qualified pediatrician, and he must be given full authority to set up well-established rules of procedure that apply to all infants, whether on private or ward service, and given authority to make sure that these rules are being followed to the letter without interruption.

Pediatric consultation is required within 24 hours (or sooner if the infant's condition demands it) for premature infants and all sick infants. It is required that all infants be examined by a physician prior to discharge from the hospital, and no infant in poor condition may be discharged. Regulations are enforced for the conduct of labor, especially those relating to obtaining consultation for complicated operative procedures by physicians who are not specialists, as recommended by the Joint Maternal Welfare Committee.

A thorough check of hospital records is made to aid, among other things, in determining when consultation as required by the regulations for the delivery of the patient is not called, so that the hospital administrator may be informed and make sure that consultation is called when it is required.

Regulations are enforced for the care of the newborn infant, both in the delivery room and the nursery. Some-

one familiar with the care of the premature infant must be present in the delivery room at the time of delivery of such an infant. Necessary equipment for caring for the infant must be available, and proper incubators for transporting these infants from the delivery room to the nursery must be provided. Revisions of the regulations are suggested by the Joint Maternal Welfare Committee as increasing knowledge shows the need.

Hospital records are studied by thoroughly competent specially trained reviewers, using a comprehensive, all-inclusive audit form to determine their completeness, accuracy and uniformity. Hospital facilities and practices are evaluated to make sure that all modern methods are utilized in the care of premature infants in hospitals, and that adequate facilities and specially trained personnel are provided. The regulations formulated and adopted by the board of health on March 15, 1938, are actively enforced, and hospital administrators are shown the necessity of compliance.

Prenatal and infant care are made available through city-wide clinics for those unable to afford a private physician. The health department makes every effort to see that adequate prenatal care is provided by demanding compliance with the regulations requiring that a complete prenatal record be filed as a part of each hospital record; by education of women in the need for early and continued prenatal care under their own physician; and by a case-finding and case-holding program to make sure that pregnant women who do not have a private physician have prenatal care early and that they return to the clinic regularly and frequently.

Homes in the lower socioeconomic groups are investigated prior to home delivery. If homes are found not to be satisfactory for deliveries, every effort is made to see that the mother is moved to a hospital. Ambulance incubators are provided when transportation of premature infants is necessary. This includes the use (established by us in 1935, and continuously in service since that time) of the first municipal transport service for premature infants who have to be quickly and safely moved from the home to the hospital or from one hospital to another. Calls are made regularly by the health department nurses and by those of the Infant Welfare Society and Visiting Nurse Association to make sure that the infants, where no private physician is in attendance, receive proper care. A physician is available for home calls on sick infants when no private physician is in attendance.

COLLECTION AND ANALYSIS OF RELIABLE STATISTICAL DATA

To determine the causes of death and all factors related thereto data were collected from postmortem examinations in 10,021 neonatal deaths, on 8,905 of which clinical investigations were also available, on births and deaths in premature infants, for 1948 to 1950, and 1950 alone, and from the scoring forms on inspections of hospitals. It is recognized that if a large group of the neonatal deaths that we studied could be proved representative of all the 18,741 deaths that occurred from 1936 to 1949, it would be possible to calculate mortality rates for individual causes of death and related factors for the total of 873,310 infants born during this period.

Mortality rates give a better and more accurate method of making comparisons and drawing conclusions than percentage distributions.

Therefore, first the 10,021 neonatal deaths with satisfactory postmortem examinations were compared with a 5% sample of the 18,741 neonatal deaths selected at random, including those with and without satisfactory postmortem examinations. The 5% sample was chosen in such a way that every infant death within a given year had an equal chance of being included in the sample, 1 out of 20 actually being included, through the use of Tippett's⁴ table of random numbers.

The 10,021 neonatal deaths were found not to be representative of all of the total deaths with respect to race, because there was a larger proportion of nonwhites in the 10,021 deaths than in the 5% random sample. The discrepancy in proportion of nonwhite infants in the 10,021 neonatal deaths and the total of 18,741 deaths was found to be limited to the 1,116 cases for which no clinical investigations were available. In this group of 1,116 cases the proportion of nonwhite infants was much larger than in the 18,741 total deaths.

However, a second comparison did reveal that the large group of 8,905 cases with satisfactory postmortem examinations in which clinical investigations were also made was representative of all the 18,741 deaths. These 8,905 cases did not differ to a significant degree from the 5% random sample in the distribution of such factors as age, sex, color, and maturity of the infants, age and gravidity of the mother, place of birth and socioeconomic area of the infant's residence, single or multiple births, fetal presentation, medical history, delivery, anesthesia, duration of labor, and complications of pregnancy.

Since the 8,905 cases were found to be representative of all deaths, mortality rates per 1,000 live births were then calculated for the total of 873,310 infants born during the 14 year period of the study with assurance of their accuracy. We found that any particular group of these 8,905 deaths, such as deaths of full-term infants or of premature infants, did not differ in any characteristic more than 1.5% from this same characteristic of the total deaths, and therefore would probably be significant in less than 3 of 1,000 instances. This is a very narrow range of statistical significance.

Tables of the factors related to the infant's mother and infant's birth obtained from clinical investigations were constructed and the material analyzed statistically. For the purpose of this presentation previable infants are defined as those weighing less than 1,000 gm., premature infants as weighing between 1,000 and 2,500 gm., and full-term infants as weighing more than 2,500 gm.

Analysis of the data on the 8,905 clinical investigations showed that by far the greatest number of infant deaths occurred on the first day of life; that the neonatal mortality rate for nonwhite infants was appreciably higher than for white infants; that the neonatal mortality rate for previable infants was 871.3 per 1,000 live births, 147.0 for premature infants, and only 8.3 for full-term infants.

Neonatal mortality rates per 1,000 live births were highest for infants born to mothers under 20 and over

4. Tippett, L. H. C.: *Random Sampling Numbers, Tracts for Computers No. 15*, London, Cambridge University Press, 1927.

40 years of age. The rate for twins was 11 times greater than for single infants. The mothers of the premature infants who died had had previous premature infants or abortions about two and one-half times oftener than the mothers of the full-term infants. As gravidity increased, the neonatal mortality rate increased.

The neonatal mortality rate for infants of mothers with toxemia was twice as high as for infants of mothers without toxemia. Among nonsurviving infants, breech presentations were more frequent in previable and premature infants than among those at term. Operative deliveries were accompanied by higher neonatal mortality rates than nonoperative deliveries. The rate for infants whose mothers received anesthetics was higher than for those whose mothers had not received anesthesia. Prolonged

TABLE 1.—Number and Percentage of Neonatal Deaths by Cause of Death, Race, and Sex, in Chicago, 1936-1949

Cause of Death	Number of Deaths								
	All Races			White			Nonwhite		
	Total	Male	Fe-male	Total	Male	Fe-male	Total	Male	Fe-male
All causes....	8,905	5,216	3,659	7,372	4,371	3,001	1,533	875	658
Abnormal pulmonary ventilation	3,590	2,301	1,586	3,145	1,881	1,264	745	423	322
Injuries at birth.....	1,482	911	571	1,225	756	469	257	155	102
Malformations.....	1,404	782	622	1,282	721	561	122	61	61
Infections....	1,197	689	508	913	532	381	284	157	127
Blood dyscrasias.....	472	277	195	415	242	173	57	35	22
Anoxia.....	337	209	128	292	179	113	45	30	15
Miscellaneous	123	74	49	100	60	40	23	14	9

Cause of Death	Percentage Distribution								
	Total	Male	Fe-male	Total	Male	Fe-male	Total	Male	Fe-male
All causes....	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Abnormal pulmonary ventilation	43.7	43.9	43.3	42.7	43.0	42.1	48.0	48.4	48.9
Injuries at birth.....	16.6	17.4	15.8	16.6	17.3	15.6	16.8	17.7	15.5
Malformations.....	15.8	14.9	17.0	17.4	16.5	18.7	8.0	7.0	9.3
Infections....	13.4	13.1	13.9	12.4	12.2	12.7	18.5	17.9	19.3
Blood dyscrasias.....	5.3	5.3	5.3	5.6	5.5	5.8	3.7	4.0	3.3
Anoxia.....	3.8	4.0	3.5	4.0	4.1	3.8	2.9	3.4	2.3
Miscellaneous	1.4	1.4	1.3	1.3	1.4	1.3	1.5	1.6	1.4

labor occurred more frequently when death resulted from birth injury than when it resulted from any other cause.

The causes of neonatal deaths were determined by a statistical analysis of 8,905 satisfactory postmortem examinations with clinical investigations. Ninety per cent of the deaths resulted from four leading causes, almost one-half (43.7%) being due to abnormal pulmonary ventilation (respiratory distress), and almost the other half (45.8%) being due to three other causes, injuries at birth (16.6%), malformations (15.8%), and infections (13.4%). The remaining one-tenth of the deaths were due to blood dyscrasias, anoxia, and miscellaneous causes (table 1).

Abnormal pulmonary ventilation was the leading cause of death (43.7%). These deaths could only be accounted for on the basis of inadequate functioning of the lungs, due to immaturity of the tissues and sometimes associated with pulmonary hyaline membrane

associated with the collapse of the walls of the alveolar ducts and most of the alveoli, called resorption atelectasis.

In congestive pulmonary failure (resorption atelectasis with hyaline-like membrane), there are distention of the capillaries, resorption of air, and the presence of a substance covering the walls of air spaces remaining open. One of us (E. L. P.) has stated⁵ that this condition is responsible in the Chicago Lying-In Hospital of the University of Chicago for more deaths of live-born infants than any other single cause. It was present as the only pathological change in 40% of all infants weighing from 1,000 to 2,500 gm. who died between 1939 and 1949. In the past year, any infant in this hospital who began to show any evidence of respiratory distress has been given oxygen in an incubator in which the humidity has been maintained at 90% to 95%. The incidence of hyaline-like membrane seems to have been markedly reduced. Whether the increase in humidity will continue to have such a striking effect remains to be seen.

Mortality rates from abnormal pulmonary ventilation were far higher among previable and premature infants than among full-term infants; the mortality rate was higher in the nonwhite than in the white infants. Most of the deaths from this cause occurred on the first day, and the mortality rate was highest following delivery by cesarean section.

Injury at birth was the second leading cause of death (16.6%). Calculated mortality rates from this cause were much higher in previable and premature than in full-term infants. Infants of younger and older mothers had higher calculated mortality rates from birth injuries. The rates with mid and high forceps and version and extraction deliveries were much higher than with other methods of delivery. Malformation was the third leading cause of death (15.8%). The calculated mortality rate was 14 times higher in the previable and nine times higher in the premature than in the full-term infants.

Infection was the fourth leading cause of death (13.4%). Pneumonia was by far the commonest form of infection, and accounted for 70% of the deaths from infection in the neonatal period. Deaths from infections were proportionately less frequent during the first day. The mortality rate from infections was twice as high in the nonwhite infants.

Blood dyscrasias caused 5.3% of the total number of deaths. Erythroblastosis accounted for 2.8%. It was three times more frequent among the white than among the nonwhite infants, was more frequent in infants at term than in premature infants, and became a commoner cause of death with increasing gravidity. Hemorrhagic disease of the newborn caused 2.4% of all deaths. Many more of the infants dying of this cause were premature than full-term or previable. Blood dyscrasias other than erythroblastosis or hemorrhagic disease of the newborn accounted for seven (0.1%) of the deaths.

Anoxia caused 3.8% of the total number of deaths. Most of the deaths from this cause occurred in the first 24 hours; the rate was higher in the white infants. The number of deaths from anoxia was highest following cesarean sections, and the rate from this cause was higher with operative than nonoperative deliveries. Miscellaneous causes accounted for only 1.4% of the total neonatal

5. Potter, E. L.: Pathology of the Fetus and the Newborn, Chicago, Year Book Publishers, Inc., 1951, pp. 249-252.

deaths. There were no abnormalities in 72.8% of previsible infants who died and 47.4% of premature infants except inability to carry on normal respiration. Deaths from injuries at birth, malformations, and infections were proportionately more frequent in full-term infants.

Slightly more deaths (51.9%) occurred during the first day of life than during the remainder of the entire first month. Of all the 13,702 deaths in the first year, 73.1% occurred during the first month. The percentage of deaths caused by injuries at birth on the first day was eight times higher than in the period from 15 to 29 days. Abnormal pulmonary ventilation was almost four times as common on the first day, while blood dyscrasias were a more frequent cause of death in the 1 to 14 day period, and deaths from infections were three times more common during the 15 to 29 day period than during the first day. Hence, one of the greatest immediate concentrations of our preventive reports must be against the many deaths from abnormal pulmonary ventilation and injuries at birth that occur on the first day.

Deaths were classified according to immediate cause of death, as well as by underlying causes. By underlying cause is meant the fundamental underlying condition responsible for death, such as a birth injury. By immediate cause is meant the acute condition that, superimposed on the underlying condition, immediately causes death, such as an infection. For example, when an infection such as meningitis was superimposed on a congenital malformation such as spina bifida, the infection was considered the immediate cause of death and the malformation as the underlying cause.

With the classification by immediate cause, malformations caused only 12.1% of neonatal deaths instead of 15.8%, as with classification by underlying causes.

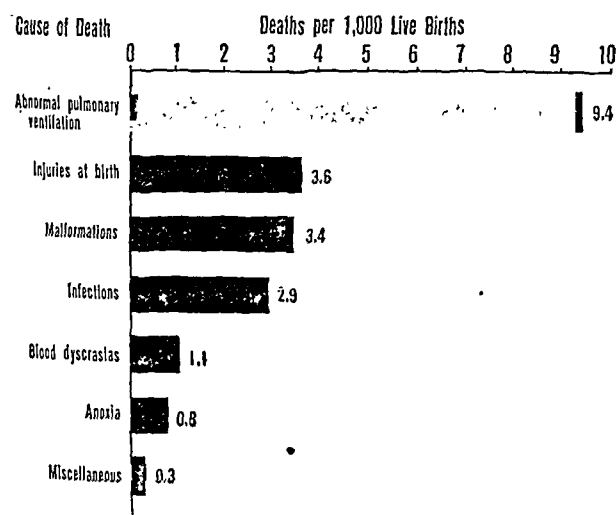


Chart 1.—Estimated neonatal mortality rate for each cause of death per 1,000 live births in Chicago, 1936-1949. The rates are based on causes of 8,905 neonatal deaths established by satisfactory postmortem examinations. These rates were then projected to the 18,741 total neonatal deaths.

Again, with the classification by immediate cause, infections caused 18.2% of all neonatal deaths instead of 13.4% by underlying causes. Miscellaneous causes accounted for 1.1% of the deaths with the classification by immediate cause, and 1.4% by underlying causes. Thus, when deaths are classified by immediate cause the num-

ber of infections increases and malformations decrease. The percentage distribution of the other causes remains about the same.

The 8,905 deaths were classified by the year in which the death occurred (1936-1949). Mortality rates were calculated for each cause for each year as well as for the

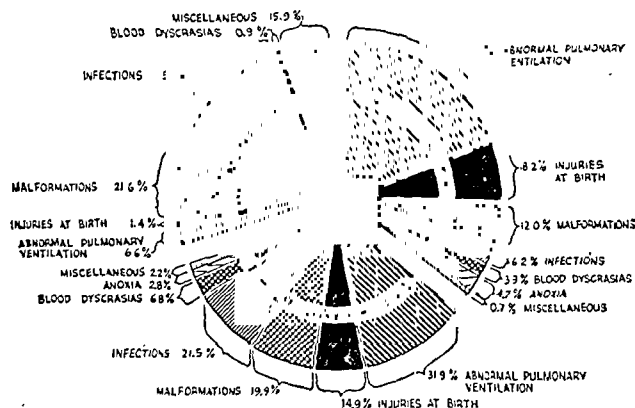


Chart 2.—Percentages of deaths by cause of infants of less than 1 day old, between 1 and 29 days old, and from 1 to 11 months old in Chicago, 1936-1949.

14 year period, for the total of 873,310 births. The mortality rate for full-term infants from abnormal pulmonary ventilation was 1.8 per 1,000 live births as opposed to 596 per 1,000 live births for previsible infants. The calculated neonatal mortality rates per 1,000 live births for causes of death among the 873,310 infants born during the period of study were abnormal pulmonary ventilation, 9.4; injuries at birth, 3.6; malformations, 3.4; infections, 2.9; blood dyscrasias, 1.1; anoxia, 0.8, and miscellaneous, 0.3 (chart 1).

Neonatal mortality rates from infections up to the present writing have not shown any appreciable decrease even with the introduction of the sulfonamide drugs and the antibiotics. The neonatal mortality rate from injuries at birth decreased during the 14 year period. Deaths from miscellaneous causes decreased, while those from anoxia increased.

A higher mortality rate among the nonwhites than among the whites was noted for every year. This was due to the increased number of deaths from abnormal pulmonary ventilation, injuries at birth, and infections among the nonwhite infants. A marked increase (8.6% in 1936 to 21.4% in 1951) in the percentage of nonwhite births as well as in the total number of nonwhite births in Chicago occurred as a result of the immigration of nonwhite persons of childbearing age. In 1951, of premature infants weighing from 750 to 2,250 gm., 34% were of nonwhite races. Among full-term infants only 17% were nonwhite. Hence, special effort must be made to reduce mortality rates among the nonwhite infants, particularly among smaller premature infants, if total mortality rates are to be appreciably affected.

The 8,905 deaths were classified by residence in 935 census tracts in Chicago, and grouped into five socioeconomic areas based on median rental values, percentage of professional workers, amount of education completed, and percentage of nonwhite persons in the area. These bases for determining socioeconomic status were

established by the Chicago Community Inventory of the University of Chicago. This classification showed that, with improved socioeconomic status, the white and non-white infant mortality rates, both during the first year and the first month, decrease. Higher mortality rates among the nonwhite population would seem to be more closely related to lower socioeconomic status than to their race.

The leading cause of post-neonatal deaths was infections, accounting for 53.6% of all post-neonatal deaths, with 62.6% of these infections being pneumonia. (Infections accounted for only 13.4% of the neonatal deaths.) Malformations during the post-neonatal period were second with 21.6%; miscellaneous, 15.9%; abnormal pulmonary ventilation, 6.6%; injuries at birth, 1.4%, and blood dyscrasias, 0.9% (chart 2). The chief effort post-neonatally must be in the prevention and prompt, adequate treatment of infections, especially upper respiratory conditions.

Premature births and deaths for 1948 through 1950, and 1950 alone, were classified by weight groups. During 1948 and 1949, only premature infants weighing less

TABLE 2.—Number and Percentage of Births, Neonatal Deaths, and Survivals of Premature Infants by 250 Gram Weight Groups in Chicago in 1950

Weight Groups, Gm.	Number Born	Percentage of Total Born	Number Died Neonatally	Percentage Survived One Month	Percentage of Total Deaths
Total.....	6,387	100.0	1,081	83.1	100.0
Under 750.....	257	4.0	253	1.6	23.4
750- 999.....	231	3.6	196	15.2	18.1
1,000-1,249.....	239	3.7	145	39.3	13.4
1,250-1,499.....	283	4.5	127	55.9	11.8
1,500-1,749.....	453	7.1	114	74.8	10.6
1,750-1,999.....	770	12.1	101	86.9	5.3
2,000-2,249.....	1,223	19.2	74	94.0	6.8
2,250-2,500.....	2,926	45.8	71	97.6	6.6
2,500 and over.....	72,165	91.9 *	410	99.4	28.9 *

* Percentage of all births and all deaths.

than 5 lb. (2,250 gm.) at birth were reported to the health department. Therefore, the classification for 1948 through 1950 includes only premature infants weighing less than 5 lb., while the classification for 1950 alone includes all infants weighing less than 5½ lb. (2,500 gm.). Almost two-thirds of the deaths in the neonatal period occurred in premature infants, including previable infants.

Although premature infants weighing between 2,250 and 2,500 gm. made up over 45.8% of all premature births, only 2.4% of these infants died (table 2). The survival rate was less for the nonwhite than the white premature infants of lower weights, and as the infants' birth weights increased, the percentage of deaths from abnormal pulmonary ventilation decreased, while the percentage of births from malformations, blood dyscrasias, and miscellaneous causes increased. Hence, the greatest concentration of effort must be on previable infants and premature infants of lesser weights. The leading cause of death in postmature infants (birth weight more than 8½ lb. [4,250 gm.]) was injury at birth.

A real awakening occurred to us in the health department from a critical self-analysis and reevaluation of our efforts to determine wherein we of the department were not as critical of our own activities as we were about

looking into the faults and shortcomings in hospitals.

A large mass of data was obtained on the physical setup, procedures, personnel, equipment, facilities, and policies in Chicago's hospitals with maternity divisions, and on the case records. We felt that one of the main reasons the neonatal mortality rate was not reduced was that there was not complete and satisfactory compliance with the regulations. Our survey teams were not sufficiently indoctrinated in the proper performance of comprehensive, all-inclusive hospital inspections using a complete audit and scoring system, nor in the beginning was there assigned to these endeavors a specially interested group of well-informed workers who appreciated and understood the problem.

In addition, there was need to enforce the regulations and ordinances which required that each hospital have a competent obstetric staff; that a qualified consultant be called soon enough when required and have him respond personally and immediately; that only physicians and not medical students in their clerkships, or others be permitted to deliver infants; and that adequate pediatric consultation be called at once for premature infants and for all sick infants.

Then, too, it was necessary to insist that a competent person be present in the delivery room whose primary duty was the care of the premature infant; to enforce the regulation that any deviation from any generally accepted procedures be permitted only after consultation; and to make certain that all of the newborn nursery staff was well trained, and that the nursery was under a qualified pediatrician who had the authority to see to it that these rules were carried out. It was evident that enough nurses well trained in premature care had to be provided at all times; that all infants, especially small premature infants, had to receive proper immediate postpartum care in the delivery room; and that the antepartum history had to be available in the delivery room at the time of delivery of the infant, especially when there were antepartum complications such as toxemia. An incubator that would be satisfactory in efficiently supplying oxygen, heat, and humidity was not available. However an explosion-proof incubator has now been constructed that provides adequate moisture and immediate oxygenation of the blood automatically and mechanically, encourages the start of natural breathing, provides for controlled positive and negative pressure, provides for effective aspiration of mucus and amniotic fluid from the mouth and trachea, signals instantly when the airways are obstructed, and provides fully regulated oxygen-containing atmosphere. After natural breathing is established, the atmosphere is automatically maintained at the physiologically ideal temperature and humidity levels. All examinations and treatment of the infant is done in this protective atmosphere.

The medical staff in many hospitals did not realize that every effort in behalf of any premature infant, no matter how small, was entirely justified and indeed obligatory. There is now virtual unanimity of recorded opinion that the incidence of premature births with their accompanying needless mortality could be materially reduced by wider immediate application of known and accepted methods of care. We also know there was an attitude in a certain few, but larger, institutions that it was less

important to maintain a good over-all premature service for all of these infants than to have a low death rate. Hence, they admitted to the premature nursery only those infants likely to survive, since they expected that tiny infants would usually die anyway, and this would adversely affect their premature death rate. Such neglect is not justifiable, and our own records in a large series of cases show that more than 14% of these previable infants survive for at least 30 days.

In many instances proper methods of resuscitation were not used. Anesthesia was not properly administered for only as long as necessary, and then only by a person with inadequate training. The regulation that oxytocics be employed in the first and second stage of labor only by certified specialists or after consultation with such specialists was not enforced. Furthermore, every hospital at all times did not have all the necessary facilities and equipment in the maternity division and newborn nursery for the proper care of mothers and infants, such as an adequate supply of blood and facilities for emergency transfusion that could not be diverted to other uses in the hospital. The graduate nurse in charge of the newborn nursery was not always competent, efficient, a leader and an executive. The premature infant was not properly and promptly transferred from the delivery room to the premature nursery.

Those women with no private physician, particularly those in the lower socioeconomic group and those with a history of toxemia, previous abortions or premature births, needed special prenatal care. An active case-finding and case-holding system had to be established for those women indifferent concerning prenatal care. Knowledge of the exact causes of death had to be acquired. The number and causes of infant deaths every month in every hospital had to be determined so that we would know when mortality rates were too high and could concentrate on those hospitals where breakdowns were occurring, and cooperate with hospitals in making necessary corrections, not just once a year, but month-by-month. Infants born at home had to be followed up early and thoroughly when a private physician was not in attendance. Those women delivering at home in a poor environment needed attention.

The quality of hospital records is an excellent index of existing conditions and quality of care in a hospital.⁶ With accurate, complete records, errors and defects in hospital management can be more easily detected. The employment of a record auditor in hospitals is of inestimable value in securing satisfactory records, and a record auditor is now being added to our survey teams of the health department. It is his function to survey and audit conditions in hospitals on the basis of their records, and where records are faulty, to have them made more accurate and complete. Action was required to make hospital records accurate, adequate, and complete. We knew that, at times, the attitude of some hospital staffs toward records indicated that they believed that "they did not have time to bother with records when they had to see so many patients." Until this improper attitude was corrected, records continued to be faulty, misleading, and inaccurate.

We have made a careful study of the procedures in hospitals as well as in the health department, and a sta-

tistical analysis of the factors related to the infant's mother and the infant's birth, and an analysis of the causes of death. From this study and from a statistical analysis of our data, it was possible better to determine the special role that the health officer, obstetrician, pediatrician, hospital administrator, nursing personnel, and others could play in reducing neonatal mortality, especially when working closely together.

COMMENT

The continued needlessly high neonatal mortality rate must be regarded as a national reproach. The health officer has a vital role in reducing neonatal mortality. He has an obligation to enforce the regulations for improving the quality of care of mothers and their infants, particularly in hospitals. He must set up a program to fulfill this obligation and make sure that the program is completely carried out. Definite objectives must be established, a course of action determined for attaining those objectives, necessary data accumulated, and action taken on the basis of these data. The health officer must make operative an audit and scoring system for detecting violations and checking the efficiency of hospitals, and a similar audit and scoring system for checking his own competency and that of his employees. He must wholeheartedly cooperate with the obstetrician, pediatrician, nurse, hospital administrator, nutritionist and social service agencies, since working jointly they all have a vital role in the reduction of neonatal mortality. Unless each of these assumes his part and unless they all cooperate wholeheartedly, a maximum reduction of neonatal mortality cannot be attained.

Collection, compilation, and careful analysis of data that reveal the exact causes of death and all the related factors for such deaths, such as race, gravidity, and toxemia of pregnancy, are important in determining the course of action needed to reduce neonatal mortality, and these data are presented here. A special effort must be made to determine the cause of pulmonary hyaline membrane (a common cause for respiratory distress) and to devise methods for promptly diagnosing and treating this condition. Deaths from injuries at birth have by no means reached an irreducible minimum and continued efforts to provide skillful obstetric care must be exerted. Greater effort must be placed on early detection of infants with infections and promptly placing them under proper treatment, both neonatally and post-neonatally. Better methods must be devised for the treatment of anoxic infants and for the prevention of conditions, such as prolonged labor, that lead to anoxia.

There is need for investigation to determine the causes for and methods of prevention of premature births, possible ways of preventing erythroblastosis, the effects of nutrition of the pregnant woman on the occurrence of prematurity and malformations, and the relation of socioeconomic status to infant mortality.

To reduce neonatal mortality effectively, the greatest effort must be concentrated on the first day of life, when most of the deaths occur; on premature infants of lower weights who are responsible for a great share of neonatal mortality; on correcting conditions in hospitals respon-

6. Annual Report of the New York Academy of Medicine, 1950. Published by The New York Academy of Medicine, New York, N. Y.

sible for these deaths, such as lack of proper care in the delivery room, and failure to provide oxygen, heat, and adequate humidity, and on mothers of the lower socioeconomic groups, particularly the nonwhite mothers whose infants contribute so greatly to the ranks of those dying needlessly.

Proportionately more deaths occur among the non-white premature infants than among the white from abnormal pulmonary ventilation, injuries at birth, and infections. Hence, for a reduction in neonatal mortality where the nonwhite population is large, efforts must be concentrated particularly on these three causes in the nonwhite group, in those of lower socioeconomic status, and in illegitimate births. These efforts should include provision of more skilled obstetric care, improvement in home conditions for those in the lower socioeconomic groups, closer follow-up by nurses to make sure that all neglected infants receive early adequate medical and nursing care, and provision of proper prenatal care for all women, especially those of lower socioeconomic status.

SUMMARY AND CONCLUSIONS

Our statistical analyses and study of our activities demonstrated to us that the health officer can and must play an important part in reducing neonatal mortality by formulating and enforcing regulations for controlling hospital procedures, facilities and personnel; by amassing and disseminating accurate information from the medical literature concerning the newer methods of preventing neonatal deaths as well as increasing familiarity with the already tried and proved ones; by calling attention of physicians to the many preventable hazards of pregnancy as shown by statistical studies, such as those included here; by exchanging information concerning successful procedures at meetings with obstetricians, pediatricians, and others; by employing proved health educational measures; and by stressing the need for making available vitamin and mineral supplements as indicated, particularly to women of the lower socioeconomic groups.

The health officer can also help reduce deaths in premature infants by seeing that medical and nursing forces concerned with the care of these infants are fully prepared constantly to meet every emergency and that measures to prevent prematurity, such as the use of progesterone, are widely employed. The health officer can aid in controlling congenital syphilis by educating women to report to a physician early in pregnancy; by making every effort to find women and men infected with syphilis; by making sure that all persons with established diagnoses of syphilis receive necessary treatment; and that treatment of the pregnant women is continued until it is certain that the fetus is completely protected.

The obstetrician in helping to reduce neonatal mortality must have the complete cooperation of the health officer in seeing to it that proper facilities are provided, so that the obstetrician may be able more efficiently to do his job of giving the best possible prenatal, natal, and postpartum care. Proper delivery techniques, proper use of analgesics, anesthetics and oxytocics, and regulations

to control the use of these three agents are important. In the prevention of prematurity, adequate prenatal care is needed as well as proper treatment of threatened abortions.

In the prevention of injuries at birth, it is important, according to our data, that all labors and deliveries, and especially premature labor and delivery, be properly conducted. To help prevent neonatal mortality from pneumonia, in prolonged labor, or after early rupture of the membranes, a well-accepted procedure is, as a rule, to give an antibiotic to the mother prior to delivery and to the infant after birth. Joint action by the health officer and obstetrician can assure that all well-accepted procedures are utilized.

The pediatrician, acting jointly with the obstetrician and the health officer, can assure proper care of the premature infant, including the provision of adequate humidity, oxygen, and heat. The provision of adequate humidity (65%) for smaller premature infants has been stressed by Schwentker and others,⁷ and even 90 to 95% for those with pulmonary hyaline membrane. High humidity is especially important in the treatment of those infants suffering from congestive pulmonary failure (resorption atelectasis with hyaline-like membrane). This condition may be primarily a pediatric problem, for it is not seen in infants who die within one hour of birth or in those who survive more than one week.

In preventing deaths from erythroblastosis there is need for diagnosis prior to the delivery of the infant. Such a diagnosis is possible by making a test for antibodies in the mother. When the birth of an infant with erythroblastosis is expected (and it is estimated that this occurs once in about every 300 births), preparations must be made immediately to transfuse the infant or even to carry out an exchange transfusion.

The prevention of deaths after the first month is also a joint pediatric and health department problem. The majority of post-neonatal deaths are due to infections contracted at home, and can often be prevented by discovering sick infants through health department nurses' visits, where no private physician is in attendance, and making sure that these infants are promptly and properly treated.

The nursing personnel of the hospital can aid greatly in reducing neonatal mortality by making sure that every infant receives the best possible nursing care without interruption throughout the 24 hour period of each day. Nurses must be well trained to recognize symptoms indicating the need for prompt medical attention, especially in premature infants, and should not be dilatory in seeing that such medical attention is called. Working with the chief of the obstetric division and the pediatrician, they can help to be sure consultation is called when indicated. The nursing supervisor, just as the obstetrician and pediatrician in charge of their respective divisions, must be given full authority to establish rules of procedure for nurses under her direction, and have the power to enforce these rules.

The hospital administrator, to aid in reducing neonatal mortality, must make sure that personnel, procedures, equipment, and facilities of the institution under his direction constantly comply with the health department requirements.

7. Schwentker, F. F.: The Treatment of Pneumonia in Children, J. South Carolina M. A. 46: 69-72 (March) 1950.

The nutritionist can jointly with the health officer and physician disseminate information concerning adequate diets for pregnant women, and the need for early administration of vitamin and mineral supplements, particularly to those women of lower socioeconomic status. There seems to be some relationship between the diet and the occurrence of prematurity. In some way poor diet and prematurity go hand in hand. There seems to be fewer premature births among women who receive diets especially rich in minerals and vitamins. There is less prematurity among women who receive an adequate diet during pregnancy. The kind and amount of work the mother does also seems to be related to premature labor.

Social service agencies have a part in reducing neonatal mortality by assuring adequate funds for providing medical and nursing care to the indigent, and proper housing and food for the pregnant women in the lower socioeconomic groups. Increased mortality rates among those of

lower socioeconomic status may be due to an increased number of premature births in this group. Eastman,⁸ an outstanding authority on this subject, believes this is based on the general characteristics of people in this group, who habitually neglect to seek prenatal care though it is known to be available and who, as a rule, are shiftless and improvident with ill-managed habits of living.

Our study and analyses have demonstrated the direction of effort by all concerned needed to prevent needless neonatal deaths. Primarily, the health department must re-double its effort to assure optimum care for all mothers and their newborn infants to assure the use of modern, accepted methods of treatment for all premature infants, and the best possible obstetric care during delivery.

54 W. Hubbard St. (Dr. Bundesen).

8. Eastman, N. J.: Prematurity from the Viewpoint of the Obstetrician, *Am. Pract.* 1: 343-352 (March) 1947.

HYSTEROSCOPE IN DIAGNOSIS OF PATHOLOGICAL CONDITIONS OF UTERINE CANAL

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Direct observation of the uterine canal with the lens hysteroscope¹ is a relatively simple procedure. After the examiner becomes accustomed to various appearances of the endometrium, as seen through the hysteroscope, the examination is not too difficult. Also, taking into consideration that the field of vision is magnified to a certain extent, the examiner will not be misled as to probable pathological conditions in the findings of either normal endometrium or endometrial hyperplasia.

Since uterine bleeding is a common complaint, and at times one of the most difficult to diagnose as to the cause of bleeding, it would seem that an instrument, such as the hysteroscope, for direct vision would be of value, not only in diagnosis but also in the treatment of certain pathological conditions of the uterine canal. So often in patients with uterine bleeding there is normal bimanual findings that it is assumed that the cause of irregular bleeding is functional in origin. If the basal metabolic rate is normal, the patient is advised to have a curettage, which so often will miss benign and malignant lesions of the uterine canal. Suction biopsy or Papanicolaou stain, if negative, is still not conclusive as to the presence or absence of malignancy of the endometrium. It is estimated that the curette will miss about 30% of the carcinomas of the endometrium, while Papanicolaou stain taken from the vaginal vault will miss roughly about 25%. Suction biopsy, of course, is more accurate. Since the cause in a high percentage of patients with uterine bleeding is found in the uterine canal, it would seem advantageous that all means available should be used in diagnosing such bleeding.

The four most frequent pathological findings of the uterine canal are endometrial hyperplasia, polyps of the uterine canal, submucosal myoma, and carcinoma of the endometrium. Unlike other organs of the body, there is

interwoven and overlapping benign and malignant lesions of the canal, such as the association of polyps, submucosal myomas, and endometrial hyperplasia with carcinoma of the fundus. Many authors state that fibroids are associated with carcinoma of the endometrium in percentages ranging from 20% to 40%. Carcinoma of the endometrium is often seen developing in the mucous membrane covering a submucous fibroid, so that the diagnosis of fibroids of the uterus as a causative factor of uterine bleeding, whether these fibroids are palpated on the serosal surface or are diagnosed with the curette as a submucosal myoma, should not be taken as a cause of bleeding, particularly if the patient is near menopause age. The same may be said of polyps of the endometrium when there is no definite proof that these polyps become malignant, as they do in other portions of the body. However, it is a well-known fact that patients having carcinoma of the endometrium often have multiple polypoid growths also, so that the recovery of polyps on curettage may not indicate the causative factor, since the curette may have missed an early carcinoma.

Parsons^{1a} summed up the difficulty in diagnosing early malignancy of the endometrium when he stated:

There can be no doubt that in the field of surgery for malignancy the size of the initial lesion is the most important single prognostic factor, outweighing duration of the disease and grade of the disease. It is possible within limits to measure the extent of the disease within the cervix by employing such clinical classification, but where carcinoma of the endometrium remains hidden

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1. The hysteroscope is manufactured by the National Electric Instrument Company.

1a. Parsons, L.: Carcinoma of Endometrium in *Monographs on Surgery*, New York, Thomas Nelson & Sons, 1950, p. 231.

within a blind cavity such as the uterine canal, where it can neither be seen nor felt, we have no conception of the site of the malignancy, much less its size.

Norris and Dunne² state that one-third of the carcinomas of the endometrium are not recognized prior to surgery. A very high percentage of patients with carcinoma of the endometrium recover if diagnosed early, yet 3,000 to 4,000 women die annually from carcinoma of the endometrium, due partially to their failure to consult their physician and also to the lack of accurate diagnosis on the part of the physician. Direct vision with means to take biopsy specimens should be indicated in abnormalities involving the uterus more than any other organ.

There are certain characteristics of the history of the patient with carcinoma of the endometrium that oftentimes give an indication of malignancy. It has been noted that this type of patient tends to be of the obese type, and in a fairly high percentage diabetes is associated with carcinoma of the endometrium, probably because of the overweight rather than the fact that the patient has a malignancy of the endometrium. Also a history of marked delay in menopause is of some significance in the diagnosis of carcinoma of the endometrium. The past menstrual history of these patients is that they had rather profuse or irregular bleeding over a period of years, with probably repeated curettages many years previously. The same history is obtained among those in whom carcinoma of the fundus develops in the postmenopausal period. In patients with such a history the development of carcinoma within the uterus is about three times the normal expectancy. Uterine bleeding is the commonest symptom of carcinoma of the endometrium in the premenopausal period and occurs as the first symptom in about 80% of the patients. However, in the postmenopausal period vaginal bleeding is the commonest symptom but usually is not so profuse as in the premenopausal carcinomatous patient and is of different character. The postmenopausal bleeding is usually slight spotting after defecation or micturition.

After routine physical examination of the patient with uterine bleeding, an x-ray, or hystero-gram, of the uterine canal is advised, in an attempt to detect any tumor, either benign or malignant, of the canal. If there is a filling defect shown in the x-ray, direct observation by the lens hysteroscope and the taking of a biopsy specimen under direct vision is done as an aid in the diagnosis of the cause of bleeding. The x-ray, or hystero-gram, is made in the x-ray department. The patient is put in the lithotomy position and properly draped with sterile drapes. The operator wears a sterile gown and gloves. The vulva is cleansed well and a speculum is inserted in the vaginal vault, the vault having been well cleansed with two applications of thimerosal (merthiolate®). The cervix is then brought into view, and a cannula with a plastic tip is inserted into the cervical canal, after which an aqueous dye is instilled into the canal. It is best that an aqueous dye be used, in preference to an oily dye; it is much less dense and will not overshadow any pathological condition in the uterine canal. If the patient complains of the slightest discomfort, which indicates that the uterine canal has been fully distended, instillation of the dye is

stopped immediately. An x-ray is made at this time, after which the cannula is removed, allowing the dye to drain into the vaginal vault. A second x-ray is made to determine if there is any retention of dye, or to outline any small polyp that might be overshadowed by the fully distended canal. If it is kept in mind that the appearance of a normal x-ray of the uterine canal is that of an inverted triangle, the base being upward, it is not difficult to detect any filling defect that might be protruding into the uterine canal. Endometrial hyperplasia, polyps, submucosal myomas, and carcinoma of the endometrium are the commonest causes of the filling defects shown in the x-ray. However, it is impossible from an x-ray alone to determine which of these is the cause of the filling defect. This is due to the fact that endometrial hyperplasia will cause a filling defect which will simulate either a polyp, submucosal myoma, or cancer of the endometrium. The object of the x-ray is only to determine if there is a filling defect. If there is no filling defect revealed on the x-ray, direct vision by the hysteroscope is not done. However, no diagnosis is based on the x-ray alone because of the variations in the pattern that might be seen in endometrial hyperplasia. In those patients with submucosal myoma the size of the myoma cannot be determined by the amount of displacement of the dye shown in the x-ray. At times a large submucosal myoma may be protruding only to a slight extent into the uterine canal and may cause only a slight filling defect. On the other hand, a small myoma may have its greatest protrusion into the uterine canal, instead of the muscle of the uterus, and cause a much greater defect in the x-ray. Hyperplasia of the endometrium on x-ray usually shows a feathery-edge outline that stops abruptly at the internal os, in contrast to extensive carcinoma of the endometrium which simulates hyperplasia in appearance but shows a protrusion through the internal os down into the cervical canal. Multiple serosal fibroids that are palpated on the serosal surface at the time of the original examination of the patient with uterine bleeding may not have any bearing as a causative factor of the bleeding. If those patients with multiple serosal fibroids are found on x-ray examination to have a normal uterine cavity, other causes of uterine bleeding should be sought, due to the fact that unless the fibroids protrude into the uterine canal they are probably not the cause of the bleeding.

In patients with carcinoma of the endometrium the filling defect is usually near the cornu, although it may be further down in the uterine canal. However, in the x-ray carcinoma of the endometrium in its early stages very closely resembles endometrial hyperplasia. The day after a filling defect is found in the x-ray, the patient has a hysteroscopic, or direct vision, examination of the uterine canal, and biopsy specimens are taken under direct vision, if thought necessary.

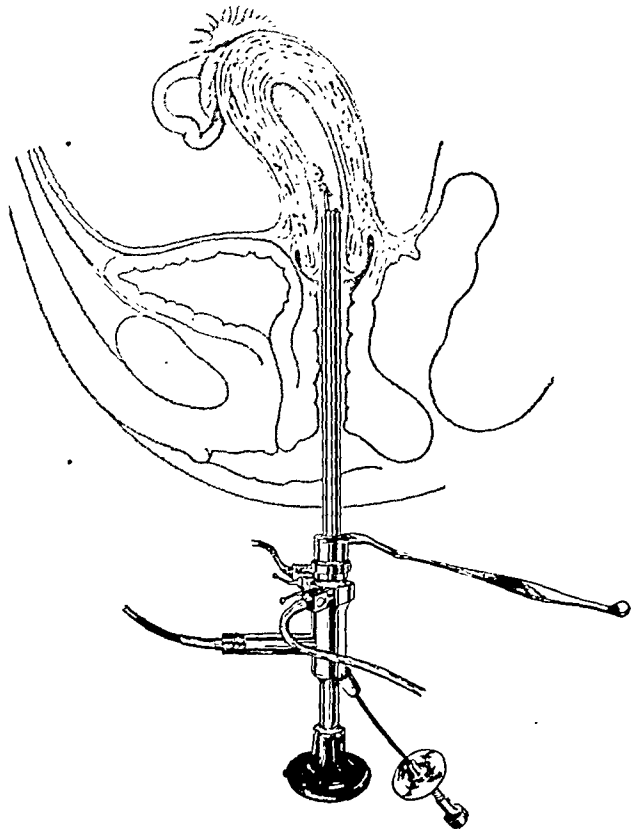
The water hysteroscope that I use at present is a direct lens vision hysteroscope, which has a compartment for an intake of water to bathe the distal lens and keep it well cleansed from blood and also an outlet to carry away blood, particles of endometrium, and debris. The water flows over the distal lens in such a manner that it is completely bathed in water, so that there is very little difficulty in blood becoming lodged and obscuring vision.

2. Norris, C. C., and Dunne, F. S.: Quoted by Parsons, L.: *Monographs on Surgery*, New York, Thomas Nelson & Sons, 1950, p. 233.

This lens system with the water intake and outflow is encased in an outer metal sheath, similar to a urethroscope for males. The outer metal sheath contains an obturator and is inserted into the uterine canal after dilatation of the canal. Previous to hysteroscopic examination, the patient's vulva is shaved. An opiate is given before the patient is brought to the operating room. The patient is put in the lithotomy position similar to that for a dilatation and curettage of the uterus. The vaginal vault is well cleansed with soap and water, and two layers of thimerosal and sterile drapes are applied. Vaginal examination is then made to be sure that the uterus is freely movable and not fixed posteriorly. If for some reason the uterus is fixed posteriorly and is markedly retroflexed, a hysteroscopic examination is not done. However, in the average uterus, which is freely movable, after dilatation of the cervix by Goodell dilators, in preference to uterine sounds, the outer sheath with the obturator is inserted into the cervical canal just past the internal os. The obturator is then removed, leaving intact the metal sheath in the uterine canal. The lens system is then inserted, locked in position, and the water intake and outflow attached, after which the light attachment is connected. The water intake is attached to a container slightly above the level of the patient, so that there will be very little pressure in the uterine canal. The tubing leading from the water outlet is either immersed in a basin of water to promote siphonage or connected with very slight suction, since strong suction tends to produce further bleeding. Water is then allowed to flow into the uterine canal for a period of a few seconds, and the suction, or siphonage, is allowed to drain for a short time. The suction is then immediately cut off, and observation of the uterine canal just inside the internal os is made. Here will be seen bulging down from the superior wall a convex protrusion, which will disappear when a sufficient amount of water has been allowed to flow into the uterine canal. The cause of the convex protrusion in this area is due to the sagging down of the superior wall of the uterine canal, which at first appearance simulates a submucosal fibroid. As the water flows in freely and dilates the uterine canal, this convex protrusion will quickly disappear. After the dilatation of the uterine canal by water distention, distal to the internal os will be noticed a more or less ragged collar outline of floating endometrium that has been raised by the slight trauma caused by the outer sheath entering the uterine canal in this area. Since this is the narrowest portion of the uterine canal proper, there will be seen more endometrium or shreds of endometrium floating in the water in this area than in the fundus of the uterus. However, this should not be taken as of any pathological significance. As the hysteroscope is carried further into the uterine canal, it will be seen that small shreds of endometrium are floating in the water, some very light in color due to the reflection of light on the strands of endometrium. At this stage of the examination it will be found that there is plenty of room for observation of the uterine canal, since the water tends to hold open the canal, permitting accurate examination of the entire canal, including its cornu. The general appearance of the uterine canal at the upper portion depends entirely on the amount of hyperplasia of the endometrium contained in the canal. In some of the

examinations it will be found that the entire canal is covered with strand-like particles of endometrium floating in the water, giving a moss-like appearance, while in other examinations, particularly at the top of the uterine canal, very smooth areas may be found devoid entirely of these finger-like projections. If there are any small blood clots retained in the canal, they will be bluish.

The best vision through the hysteroscope is obtained when the distal lens is about 1 in. or more away from the endometrium. If at this stage of the examination the vision becomes blurred, it is probably due to one of several causes. Either the hysteroscope is in too close proximity to the endometrium or the water is becoming too stained with blood and needs replenishing. Occasionally vapor will collect on the proximal lens and needs to be wiped off with dry gauze. Rarely will blood clots or debris



Hysteroscope inserted in uterine canal demonstrating taking of biopsy specimen under direct vision. Continuous flow of water bathes distal lens, insuring clear vision.

collect on the distal lens, even in those uteri containing much blood. Since the size of the uterine canal is relatively small, much of the observation of the entire canal can be made with a few changes of water. This, of course, depends on how much uterine bleeding there is at the time of the examination. With those patients with moderate amount of bleeding, two to three instillations of water are sufficient for complete examination of the uterine canal. With those patients bleeding profusely, the water will have to be replenished every few seconds to get clear observation. The most important caution to keep in mind is that the outflow of water is cut off at the time of observation.

Since we are accustomed to seeing the uterine canal in the usual specimen as being very smooth in appear-

ance, it is surprising at times on first observation through the hysteroscope to see small particles of endometrium floating in the water, giving the uterine canal the appearance of being very ragged, in contrast to the specimen when it is removed. With the area of the uterine canal which showed the filling defect on previous x-ray examination kept in mind, the hysteroscope is carried to this area of the canal, and a careful examination as to the cause of the filling defect, which may be due either to endometrial hyperplasia, polyps, submucosal myomas, or carcinoma of the endometrium, is made. After examination of the canal is completed and biopsy specimens are taken, when indicated under vision, the examination, of the cervical canal is made before the entire examination is completed. When the hysteroscope is withdrawn down beyond the internal os and observation of the cervical canal is made, it will be seen to be very white in contrast to the uterine canal proper. I believe that this type of examination with the hysteroscope is more accurate than use of the curette, and also less harmful, particularly in cases of carcinoma of the endometrium, since the curette will tend to spread the carcinoma through the lymphatics by vigorous curetting. In those patients with profuse uterine bleeding I have found that giving 25 to 50 mg. of testosterone daily for three days previous to hysteroscopic examination will aid a great deal in reducing the amount of bleeding, so that observation is much more distinct. The appearance of benign lesions of the uterine canal, such as polyps and submucosal myomas, shows very clearly through the hysteroscope, since these lesions are bathed free of blood by the continuous flow of water. The polyps will tend to float freely in the water, particularly if they have a small pedunculated base, and are lifted upward so that the base may be well visualized. If the polyps are not too large and do not have too wide a base, they may be fulgurated at their base by carrying a fulguration tip through the water outlet and burning off the polyp, which oftentimes is very difficult to remove with a curette.

The following is a report of a case of small polyp in the cornu, which caused continuous uterine spotting.

Mrs. F. B., 63, had her last menses at the age of 47. She had noted no spotting until the last two months but had noticed almost daily uterine spotting since then. There had been no loss of weight, no abdominal pain associated, and no discomfort in any respect. She had consulted her physician after two weeks of spotting, who advised that she have a curettage, which she postponed. She had noticed no odor associated with the uterine spotting. After two months of almost daily uterine spotting, she entered the hospital for x-ray and hysteroscopic study. A hystero-gram, or x-ray, was made showing a definite filling defect at the left cornu. Physical examination at this time revealed a fairly obese woman very healthy in appearance. Eye, ear, nose, and throat findings were normal. The thyroid was normal to palpation, and the heart and lungs were normal. There were no masses or tenderness in the abdomen. The outline of the liver edge was normal. Vaginal examination revealed a normal cervix and a normal-size, freely movable uterus; nothing was felt in the adnexae. The extremities were normal. The blood pressure was 140/80. Laboratory examination revealed the urine to be normal. The hemoglobin was 72% and the red blood cell count 3,900,000.

The age of the patient together with the almost daily uterine spotting was very suggestive of carcinoma of the endometrium, and since there was a filling defect shown on x-ray at the cornu, it was thought best to do a hysteroscopic examination and take biopsy specimens under direct vision. This was done, and the cervix was found to be entirely normal. The hysteroscope was passed to the fundus, and examination of the area that was

shown previously in the x-ray to have a filling defect revealed a long pedunculated polyp arising from the left cornu. It was very smooth in outline, which was unmistakably that of a polyp rather than a carcinoma. Since it had a small pedunculated base, the fulguration tip was carried through the water outlet, the polyp fulgurated at its base, and the base well fulgurated. Examination of the remainder of the uterine canal revealed no abnormalities. A curettage was not done. Since many of these small polyps arising from the cornu are difficult to remove with the curette, it is highly possible that this patient could have had repeated curettages with no abnormalities revealed, this treatment eventually resulting in either the application of radium or a hysterectomy.

The appearance of early carcinoma through the hysteroscope is that of a fungating pinkish growth with slight tentacles floating freely in the water. These tentacle-like projections that are held upward by the water are not seen in an area of endometrial hyperplasia, and a carcinomatous growth has become very extensive, involving the entire uterine canal, there will often be seen whitish-grey areas where necrosis has occurred, and also that the carcinoma has extended down through the internal os into the cervical canal, unlike hyperplasia, which stops abruptly at the internal os. If the suspected carcinomatous growth is an early or extensive lesion, various spot biopsy specimens may be taken under direct vision with the biopsy specimen taker. In this way, particularly with the early carcinomatous lesion of the endometrium, there will not be as much liability of missing a growth as there is when the curette is used, with which at times it is very difficult to get a specimen, particularly from the cornu.

The following case is an illustration of carcinoma of the endometrium diagnosed by use of the hysteroscope.

Mrs. A. P., 48, gave a history of spotting between menstruation for the past several months and also had noticed that the menses had become much more profuse during the past four to five months. There had been only slight odor associated with the uterine bleeding. There had been no abdominal discomfort, loss of weight, or any other complaint. Since this patient was of menopause age, she had noticed the bleeding to be much more profuse at this time; it occurred at any time during the day and not on defecation or micturition. The patient thought that the irregular bleeding was probably associated with menopause and did not give it any serious thought. A hystero-gram, or x-ray examination, was advised. Aqueous dye was instilled into the uterine canal and x-rays taken, which revealed a very ragged outline of the uterine canal with a large filling defect which was very suggestive of an extensive carcinoma of the endometrium. Physical examination revealed a robust woman. Eye, ear, nose, and throat findings were normal. The thyroid was normal to palpation. The heart and lungs were normal. There were no masses or tenderness in the abdomen. Vaginal examination revealed a normal-appearing cervix. Uterine spotting was seen at the external os at this time. The uterus was slightly enlarged and boggy; nothing was felt in the adnexae. The uterus was freely movable. The extremities were normal. The blood pressure was 160/80. Urinalysis findings were normal. The hemoglobin was 82% and the red blood cell count 4,300,000. Hysteroscopic examination was advised after the large filling defect in the uterine canal was seen in the x-ray. On hysteroscopic examination the cervical canal appeared to be normal, but just before the internal os was entered, a ragged growth protruding into the cervical canal could be seen. On passing the hysteroscope into the uterine canal, it was very evident that the patient had an extensive carcinomatous lesion involving the entire canal, with areas of whitish necrosis seen in various places. Biopsy specimens were taken which proved the diagnosis to be adenocarcinoma of the uterus.

In this case carcinoma of the endometrium was diagnosed without curettage. There was very little trauma in inserting the hysteroscope, and spot biopsy specimens could be taken at various areas.

The question of a reflux of water through the fallopian tubes during the time of the hysteroscopic examination and the possible harm that may be caused by such reflux

of water through the fallopian tubes into the abdominal cavity has been mentioned several times. However, I do not feel that a reflux of a small amount of water through the fallopian tubes into the abdominal cavity would be of any serious consequence. It is my opinion that carcinomatous cells are not carried through the fallopian tubes. Also other observers have noted that sections of fallopian tubes, in those patients with extensive carcinoma of the endometrium, have failed to reveal any carcinomatous cells in the fallopian tubes themselves.

Recently I have done hysteroscopic examinations on those patients with uterine bleeding requiring a curettage. After the curettage I inserted the hysteroscope to determine the amount of endometrium left in the uterine cavity. There could be seen areas throughout the uterine canal which the curette had missed entirely. Also it is of interest to note that in those patients with polyps of the uterine canal I found on reexamination with the hysteroscope, after locating the polyp's exact position with the hysteroscope and then curetting vigorously in this area, that the polyp was not dislodged. In those patients in whom it seems difficult to remove the endometrium entirely by curettage and in whom areas of endometrium persist in the uterine cavity, I have passed the fulguration tip to this area under direct vision and have fulgurated those areas of endometrium that remained after curettage.

On microscopic examination of sections taken from specimens after fulguration of the endometrium, it was found that the glands of the endometrium were not entirely destroyed after fulguration of the endometrium with the fulguration tip.

Follow-up on those patients having hysteroscopic examination reveals that they have very slight fever, if any,

and are discharged from the hospital usually the second day following hysteroscopic examination. There has been no untoward symptom, such as abdominal pain, tenderness, or fever, of any consequence following any hysteroscopic examination.

Those patients with uterine bleeding having an x-ray of the uterine canal, or hystero-gram, followed by hysteroscopic examination have been classed as having either negative or positive tests for tumors of the uterine canal. Those patients having a filling defect revealed by x-ray and a hysteroscopic examination in which a tumor is found to correspond to the previous x-ray finding are said to have a positive test for tumors of the uterine canal. However, if the filling defect shown on the x-ray proves on hysteroscopic examination to be endometrial hyperplasia and not a tumor, the patient is classed as having a negative test for tumors of the uterine canal.

SUMMARY

A technique of direct vision of the uterine canal by a lens hysteroscope, as an aid to diagnosing pathological conditions of the uterine canal, is described. Owing to the simplicity of the procedure, any physician can quickly acquire the technique of such an examination and will find that such procedure will aid greatly in diagnosing those tumors which are so often missed. However, it is to be emphasized that this procedure should be used in conjunction with the present methods of diagnosis of benign and malignant lesions of the uterine canal. A negative or positive test classification is suggested to describe the results of the combined x-ray and hysteroscopic examination of the uterine canal.

Jefferson Bldg.

ROLE OF PHYSICAL MEDICINE AND REHABILITATION IN A LARGE NEUROPSYCHIATRIC HOSPITAL

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By tradition, a neuropsychiatric hospital is a place where mentally ill persons may receive shelter from the stormy blasts of life, care and attention of nursing and medical auxiliaries, and the individual attention of a psychiatrist. The concept of a neuropsychiatric hospital as a refuge often means, however, that patients are robbed of their individuality and are made to become overly dependent on the meager staff employed to administer care. It is too frequently found that neuropsychiatric hospitals still adhere to the doctrine of attempting to provide individual psychotherapeutic treatment for an individual patient by an individual psychiatrist, without facing the fact that individual psychotherapy is not a practical proposition, because of the huge number of patients confronting the psychiatric world. While it is true that radical individual treatment can free the inner drives of the emotionally ill patient, it is doubtful whether the large neuropsychiatric hospital of today, with its large patient population, can function usefully as one in which individual treatment is practiced. The neuropsychiatric hospital must become a therapeutic institution in

which the auxiliary and ancillary services that are today recognized as part of the psychiatric team can function under capable psychiatric guidance. Such a concept recognizes the fact that a neuropsychiatric hospital should attempt to become a community, with the immediate aim of full participation of all patients in the daily routine and the eventual aim of resocialization of neuropsychiatric patients for life in the hospital community or in ordinary society.¹

The first neuropsychiatric hospital to integrate the psychotic within the hospital community was organized by Pinel, who, in 1792, outlined a concept for the humane treatment of the psychotic. Later, however, empha-

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is a fact that therapeutic good can and does result from work itself, if the work is constantly directed according to certain fundamental principles. Through industrial therapy, the patient can obtain the security that comes from the attention, respect, and admiration of others and can find an outlet for his creative energies through his work.⁸ Northport Hospital's gardening program was planned to include a variety of activities offering the patient who does not respond to other types of therapy an opportunity to release his aggression and hostility, and to encourage his participation on either a competitive or a passive basis. These inherent dynamic factors have resulted in development to the extent that the patients have created a garden and flower exhibit, which, in turn, has resulted in a spirit of community relationship and good-will. Gardening provides opportunities for exhibitionism, narcissistic gratification, and use of specific creative abilities, besides offering socialization values through group projects.

Corrective therapy provides physical reconditioning activities for the purpose of offsetting advance of physiological retrogression during the regressive and deteriorative phases of chronic psychosis. It is directed toward the restoration of full strength and stamina through participation in progressively graded physical activities. Corrective therapy is dynamic and psychiatrically oriented in that it insures an adequate outlet for the patient's interest and energy by satisfactorily substituting physical activity for the patient's general inactivity.⁹ Punching a bag or riding a stationary bicycle provides opportunity for release of tension, anxiety, and hostility. The ability to play with, rather than against, is encouraged. Reduction in assaultive and hyperactive states has been accomplished by this method, as attested to by the reduction in the number of patients requiring sedative hydrotherapy. Swimming as a sedative activity (with the pool heated to the proper temperature) is of great benefit for the disturbed, especially for the younger patients, who are apt to look upon swimming with favor.¹⁰

Physical therapy in a large neuropsychiatric hospital finds many fruitful applications. Hydrotherapy at the Northport Hospital is psychiatrically and physiologically oriented to the extent of being medically controlled instead of being a simple nursing procedure. It is used for treatment purposes only, is carefully observed and controlled, and the feeling of punishment is removed and restraining factors lessened by the proper training and guidance of the hydrotherapy aides. Physical therapy procedures have been found successful not only in treatment of the commoner physical disabilities but also in the treatment of functional peripheral vascular disorders resulting from hypostasis. Physical therapy is used at Northport to alleviate or prevent any physical disability.

CONCLUSIONS

For the institutional psychiatrist who finds himself overwhelmed by the responsibilities of care of a large number of patients, a physical medicine and rehabilitation service provides a laboratory where patients exposed to the modalities of such a program can be carefully observed. Contact is best established in this milieu rather than within the confines of the ward, where physically

able patients sit about deteriorating, with nothing to do, day after day, but watch others doing the same thing.

In the discussion of physical medicine and rehabilitation and its role in a large neuropsychiatric hospital, I have deliberately avoided discussing its specific psychiatric role, as in electric shock therapy, insulin shock therapy, or psychosurgery, but have confined my discussion to general facts and to its role in the medical care of the continued-treatment or chronic psychotic. Its role in the acute or early psychoses, its rehabilitation potential for electric shock therapy and insulin shock therapy, and its value in restimulation, remotivation, and reeducation of the psychosurgical case are readily accepted. It is because of the scarcity of institutional psychiatrists that I have attempted to show that physical medicine and rehabilitation, while requiring less individual attention from the psychiatrist, is dynamic and psychiatrically oriented; with it we are able to apply accepted psychotherapeutic techniques under psychiatric guidance. The basic concept of physical medicine and rehabilitation for neuropsychiatric patients has been adequately expressed by the late Dr. Burlingame, who stated, "Sound physical medicine and psychotherapy in the form of personal tutoring occupy the front ranks in the help which may be offered to the mentally ill."¹¹

It is also felt that a physical medicine and rehabilitation service in a neuropsychiatric hospital will assist in changing the ordinary conception of a psychiatric institution to one in which it is realized that "each individual patient will acquire habits and skills that will contribute to his social and economic integration."¹²

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Hemophilia in the Female.—In 1886 Treves described a family of haemophilics in which some females appeared to be affected. This family, of which the most recent report up to the present was that of Handley and Nussbrecher (1935), has been investigated again, and the inheritance of the disease has been traced to the seventh generation.

The clinical history and laboratory findings are those of haemophilia. The affected female members of the fifth generation have all the clinical and laboratory manifestations of the disease. The severity of the clinical syndrome and the degree of haematological abnormality in these women do not appear to be different from those found in the affected male members of the family. Since they were the children of a male haemophilic and his first cousin, this unusual occurrence of affected female members in a haemophilic family can be explained by assuming that their mother was a carrier, and that they were homozygous for the disease. . . . The subsequent generations are all compatible with a diagnosis of the homozygous haemophilic state in the affected women, who appear to be the first human female subjects in whom the diagnosis of haemophilia has been substantiated. Treve's original diagnosis of haemophilia in the female would thus appear to be correct.—Clarence Merskey, M.D., The Occurrence of Haemophilia in the Human Female, *Quarterly Journal of Medicine*, July, 1951.

UNRECOGNIZED PROSTATISM

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The diagnosis of prostatic obstruction ordinarily presents little difficulty. It has long been known, however, that advanced degrees of bladder neck obstruction occasionally develop so quietly that the true condition may not be suspected until severe uremia is present. This is the type referred to as "silent" prostatism. Although these patients are numerically few, they are particularly important because marked changes in the bladder and upper urinary tract have usually occurred before an accurate diagnosis has been made, and therapy is correspondingly more difficult and less effective. All three of the main causes of prostatic obstruction, benign hyperplasia, fibrous contracture, and carcinoma, may, on occasion, develop in this insidious manner. Actually, some symptoms of urinary obstruction are almost always present but may be so mild that they are ignored or lightly passed over by the patient, who thus unwittingly helps delay recognition of the condition.

In a six-year period, 16 patients whose prostatic obstruction progressed in this silent manner have been studied and treated at the Lahey Clinic. All were intelligent men, the majority of whom had been seen regularly by their physicians; yet each had serious damage of the urinary tract before obstruction was detected. The purpose of this paper is to emphasize the occurrence of this mode of onset of prostatism by reviewing the salient characteristics in these 16 cases, with a brief discussion of the treatment.

Ages varied from 51 to 75 years. Some patients had serious associated disease, such as arteriosclerotic heart disease, cerebrovascular disease, hypertension, and duodenal ulcer. The immediate reasons for seeking medical advice could be classified as follows: (1) development of gastrointestinal symptoms, such as nausea, vomiting, flatulence, and constipation; (2) development of symptoms resulting from severe anemia, as weakness, ease of fatigue, and dyspnea; (3) discovery of a mass in the lower abdomen by the patient or his physician; and (4) desire for a thorough medical examination prompted by symptoms or known disease unrelated to the urinary tract. Of the 16 patients studied, 6 had symptoms chiefly of the digestive tract, 2 had symptoms due primarily to anemia, 3 had a suprapubic mass found to be a distended bladder, and 5 had mild urinary symptoms elicited in the course of examinations being done primarily because of disease of other systems. None had ever had complete urinary retention, and most of them thought that they were passing normal quantities of urine without unusual difficulty. Careful questioning disclosed in all 16 at least a slight increase in urinary frequency with a weak stream and disturbances of control varying from mild terminal dribbling in most to definite enuresis in three.

On physical examination the most frequent findings relative to the urinary tract were (1) an obviously distended bladder; (2) evidence of dehydration, weight loss, uremia, and acidosis; and (3) changes in the pros-

tate as felt rectally. Thirteen of these patients were recognized by the examiner as having distended bladders, but in two obesity obscured the situation, and in one asymmetry of the full bladder led to the preliminary diagnosis of abdominal neoplasm. Only six had unmistakable signs of uremia with dehydration and acidosis; one had extensive dermatitis thought to be uremic in etiology. The other patients in this group looked remarkably well, despite the fact that 8 of these 10 had elevated blood nonprotein nitrogen levels of varying degrees. After digital rectal examination the condition in the prostate gland was recorded as a benign enlargement in 13, small and fibrous in 2, and carcinoma, subsequently proved, in 1. It was noted that the size of the prostate often appeared to have decreased considerably after several days of bladder drainage. Initial systolic and diastolic blood pressures were found to be well above normal in 13 of these 16 patients. No neurological abnormalities were found.

Laboratory studies revealed significant elevation in the blood nonprotein nitrogen in 14 of these men, their first determinations ranging from 48 mg. to 200 mg. per 100 cc. Although it could not always be proved that this azotemia was entirely due to prostatic obstruction, prostatism certainly appeared to be the major cause. Another striking laboratory finding was the degree of anemia found in most of this group. Fourteen had lower than normal hemoglobin levels, with nine having determinations under 10 gm. per 100 cc. The lowest was 5.8 gm. per 100 cc. Urine examination showed that only six patients had a definite urinary infection when first seen; the others voided grossly clear urine, which was of low specific gravity, often containing a small amount of albumin and an occasional red blood cell, white blood cell, or cast in the sediment (see table).

Roentgenologic examination included plain roentgenograms of the abdomen made on all, intravenous urograms done on six, and gastrointestinal studies carried out on three before the main pathologic condition was recognized. The plain roentgenograms disclosed little of importance save the absence of calculi, and the intravenous urograms showed either no excretion of dye or demonstrated hydronephrosis and hydroureters. In only one case, the upper urinary tract appeared normal, and in that case the bladder was markedly dilated and trabeculated.

REPORT OF CASES

CASE 1.—A 61-year-old man experienced intermittent vomiting, chiefly in the evening, associated with slight epigastric distress. Variable urinary frequency had been present for about six months. After roentgenologic study of the gastrointestinal tract by his local physician was considered inconclusive, he was referred for further study to the department of gastroenterology. There his examination showed moderate dehydration, a greatly

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distended bladder, and an enlarged benign prostate gland, Grade 2. The nonprotein nitrogen level of the blood was found to be 168 mg. per 100 cc., the creatinine 4.7 mg. per 100 cc., and the hemoglobin 7.5 gm. per 100 cc. The urine was of low specific gravity but otherwise normal. The blood pressure was 180 mm. systolic and 95 mm. diastolic.

The patient admitted that his urinary stream had not been very forceful, but he had not been at all concerned about this. Hospitalization was advised and immediate suprapubic trocar drainage carried out under local procaine anesthesia. Parenteral fluids, including sodium lactate solution, were given freely. The nonprotein nitrogen level subsequently rose to 236 mg. per 100 cc., then dropped to 85 mg. per 100 cc. and leveled off at that value. Repeat gastrointestinal roentgen study showed no intrinsic disease of the stomach or duodenum. He was discharged home

considered his urinary symptoms so minimal, he failed to return for this examination; he returned only when he noticed the lower abdominal mass.

Physical examination in the surgical section revealed an asymmetric cystic mass in the suprapubic region, and, because of the absence of urologic complaints, various gastrointestinal lesions were considered as possible causes. Rectal examination showed an enlarged prostate, Grade 2, which felt benign. The blood nonprotein nitrogen level was 31 mg. per 100 cc. The hemoglobin was 11.8 gm. per 100 cc., and urinalysis disclosed no abnormalities. The blood pressure was 180 mm. systolic and 104 mm. diastolic.

Barium enema roentgen study was negative for intrinsic disease of the bowel but showed compression of the sigmoid colon by the mass. An excretory urogram showed nonfunction of the left

"Silent" Prostatism; Data on 16 Patients

Case	Type of Obstruction	Chief Signs and Symptoms Prompting Examination	Admission		Urine	Type of Drainage	Type of Prostatectomy and Weight of Tissue Removed
			Hgb. Gm./100 Cc.	N P N Mg./100 Cc.			
1	Benign prostatic hypertrophy	Gastrointestinal	7.5	168	Uninfected	Trocar suprapubic	Suprapubic enucleation, 50 gm.
2	Benign prostatic hypertrophy	Discovery of suprapubic mass	11.9	31	Uninfected	Trocar suprapubic	Suprapubic enucleation, 80 gm.
3	Benign prostatic hypertrophy	Discovery of suprapubic mass	9.3	77	Infected	Urethral catheter	Transurethral resection, 62 gm.
4	Benign prostatic hypertrophy	Anemia	8.7	133	Uninfected	Trocar suprapubic	None—awaiting surgery
5	Benign prostatic hypertrophy	Mild urinary frequency and urgency; wanted general examination	8.4	115	Infected	Urethral catheter	Suprapubic enucleation, 41 gm.
6	Benign prostatic hypertrophy	Discovery of suprapubic mass	5.8	89	Uninfected	Suprapubic	Suprapubic enucleation, 44 gm. Transurethral resection, 10 gm.
7	Benign prostatic hypertrophy	Gastrointestinal; intermittent enuresis	10.9	165	Infected	Urethral, later suprapubic	Suprapubic enucleation, 52 gm.
8	Adenocarcinoma	Cardiac failure; intermittent urinary frequency	10.5	60	Uninfected	Trocar suprapubic	Transurethral resection, 10 gm., and bilateral orchiectomy
9	Benign prostatic hypertrophy	Anemia; intermittent enuresis	6.8	52	Uninfected	Trocar suprapubic	Suprapubic enucleation, 53 gm.
10	Benign prostatic hypertrophy	Gastrointestinal; intermittent enuresis	9.6	120	Infected	Urethral, later suprapubic	Suprapubic enucleation, 65 gm.
11	Benign prostatic hypertrophy	Mild urinary urgency and frequency	13.7	48	Uninfected	None	Transurethral resection, 68 gm.
12	Contracture	Gastrointestinal; mild urinary frequency	11.1	54	Uninfected	Trocar suprapubic	Transurethral resection, 14 gm.
13	Benign prostatic hypertrophy	Gastrointestinal; severe dermatitis	6.5	200	Infected	Urethral, later suprapubic	Transurethral resection, 32 gm.
14	Benign prostatic hypertrophy	Mild urinary frequency and urgency	14.1	38	Uninfected	Urethral catheter	Transurethral resection, 33 gm.
15	Benign prostatic hypertrophy	Gastrointestinal; mild urinary frequency	9.2	48	Infected	Urethral, later suprapubic	None; died in uremia
16	Contracture	Gastrointestinal	10.7	88	Uninfected	Trocar suprapubic	Transurethral resection, 8 gm.

with a larger suprapubic tube in place, and gained moderately in weight and strength. Kidney function improved slowly, but drainage had to be continued for about 15 months before he was considered a reasonably safe operative risk. At that time a suprapubic prostatectomy was carried out uneventfully, a three-lobed, benign hyperplasia being found. From the surgical standpoint he progressed satisfactorily, the wound healed normally, and he voided easily after closure of the wound; however, kidney function remained most precarious. Death occurred at home approximately five months after the prostatectomy, presumably from renal insufficiency.

CASE 2.—A 67-year-old dentist entered the clinic for examination because he had recently noted a mass in the lower portion of the abdomen. He denied having any urinary symptoms, although two and one-half years previously, while being studied in regard to mild chest pain, he had admitted having intermittent hesitancy, slight frequency, some decrease in size and force of the stream and, in fact, had been advised to have more complete urologic study, including excretory urograms. Because he con-

sidered his urinary symptoms so minimal, he failed to return for this examination; he returned only when he noticed the lower abdominal mass.

CASE 3.—A 60-year-old man said he had no urinary or other complaints whatsoever when first seen in the urology department, where he had been sent for an opinion regarding a large, lower abdominal, cystic mass, extending at least an inch above the umbilicus. The prostate was benign and enlarged to Grade 2. The urine showed five to six white blood cells per high power field and no organisms. Roentgenograms of the upper gastrointestinal tract previously made elsewhere demonstrated only distortion of the bowel pattern by the cystic mass. It was necessary to catheterize this patient and withdraw 11 oz. (330 cc.) before he could be convinced that the mass was indeed his distended bladder. The blood nonprotein nitrogen level was 77 mg. on

admission but dropped to 27 mg. per 100 cc. after urethral catheter drainage for one week. The hemoglobin was 9.3 gm. per 100 cc. The blood pressure was 190 mm. systolic and 110 mm. diastolic. Excretory urograms demonstrated bilateral hydronephrosis and hydroureters. After the kidney function had improved and the anemia was corrected, transurethral prostatectomy was carried out, with removal of 62 gm. The gland was of the trilobar benign type. Convalescence was uneventful, and the patient was discharged on the 10th postoperative day, voiding well.

CASE 4.—A 75-year-old man was admitted on the medical service because of severe weakness, nervousness, and recent nausea with intermittent vomiting. He had had mild nocturia for years but said he had no other disturbance of urinary function. His local physician had been treating him for anemia for some time, without success. Examination showed that the patient was very pale and weak; the lower part of the abdomen looked somewhat prominent, and, on palpation, the bladder was found to be distended to the umbilicus. The prostate gland as felt rectally was enlarged, Grade 3, and benign. The blood pressure was 180 mm. systolic and 90 mm. diastolic. The blood nonprotein nitrogen level was 133 mg. per 100 cc. The urine showed a rare white blood cell per high power field. The hemoglobin was 8.7 gm. and at a later examination 6.2 gm. per 100 cc. Trocar cystotomy was done under local anesthesia and the bladder emptied without incident. Kidney function improved somewhat over the next few weeks, the nonprotein nitrogen level dropping to approximately 85 mg. per 100 cc. His general condition improved slowly with hydration and numerous blood transfusions, but it became obvious that prostatectomy would have to be deferred indefinitely. He was, therefore, discharged home with suprapubic drainage, which he has tolerated well. The nonprotein nitrogen level of the blood, however, has risen to about 110 mg. per 100 cc., and the anemia becomes very severe unless frequent transfusions are given. It seems doubtful that any type of prostatectomy can be undertaken with a reasonable chance of survival.

COMMENT

The mechanism of development of this silent prostatic obstruction appears to be a conscious or unconscious stifling of the original irritative symptoms of prostatism, and, with a very gradual increase in the degree of obstruction and amount of residual urine, numbing of the sensory components of bladder innervation results. Tremendous distention of the bladder then may cause no sensation other than perhaps a vague feeling of discomfort in the lower part of the abdomen, and the urge to void may be greatly reduced in intensity or felt only as a suprapubic ache. With the overlay of digestive symptoms, such as anorexia, flatulence, and constipation, or of other disease, attention is further removed from the urinary tract, the role of the prostate being lost sight of until a thorough investigation is undertaken. Many intelligent men expect that with age some degree of urinary frequency, nocturia, and diminution in size and force of the stream constitute a normal condition, which, if not too severe, they accept as their lot and try to ignore. An underlying fear of surgical treatment also influences some persons to minimize or suppress the earlier symptoms of prostatism. Whatever the particular cause, the result may be the unrecognized development of marked urinary obstruction. With the bladder chronically distended, an overflow incontinence often occurs, chiefly during sleep or relaxation, with a considerable increase in terminal dribbling. Such patients may seek relief only when the enuresis becomes annoying.

The urine remains uninfected as a rule, which contributes to the absence of symptoms. When infection does supervene, a serious crisis may be produced, with resulting acute pyelonephritis, hematuria, and further decrease in kidney function. This usually forces attention to the urinary tract and necessitates immediate treatment. Sudden hematuria in the absence of infection may act in the same manner.

The anemia which is found in the majority of these patients apparently is related to the degree of azotemia present and is caused by depression of function of the bone marrow; an inadequate diet is, of course, an additional factor in many. Donovan¹ recently reported 10 instances of severe anemia associated with chronic prostatic obstruction. Transfusion, in addition to correction of the fundamental disease of the urinary tract, is the only effective means of therapy; it seems impossible to improve the blood picture significantly in uremic patients by means of iron or other medication.

It is apparent that the diagnosis of this relatively symptomless type of prostatic obstruction is not difficult once the possibility is considered and when the condition has become advanced. The difficulty lies in recognizing such cases before irreversible pathologic changes have occurred. In this regard the free use of excretory urography in the study of patients who present even minimal obstructive urinary symptoms or have any physical findings suspicious of obstruction of the vesical neck has been of definite aid. This is fairly common practice, we realize, and well worth while.² By means of it, several instances in which bladder and ureteral damage were developing from prostatism have been detected, and the patients successfully treated, despite an almost complete lack of the usual symptoms.

Catheterization of these patients in the office as a diagnostic means should be done cautiously, if at all, especially when the urine is sterile. The fear of introducing infection, producing bleeding or complete retention, or otherwise complicating an already serious situation before provision for hospitalization has been made, are factors that influence us against the diagnostic use of the urethral catheter whenever significant obstruction of the bladder neck is suspected. The decision regarding the necessity for hospitalization can practically always be made without its use; in fact, a careful history and physical examination usually will suffice to make the diagnosis, and further studies can be deferred until the patient is hospitalized. Then, if the kidney function is not too badly damaged, an intravenous urogram will give accurate information without requiring instrumentation of any kind.

It is important to recall that the size of the prostate on rectal examination can be misleading; a normal gland palpated rectally or one smaller than normal is not

1. Donovan, H.: Severe Anaemia and Hyperpiesia Associated with Prostatic Obstruction, *Brit. J. Urol.* 19: 126 (Sept.) 1947.

2. Engel, W. J.: Intravenous Urography in Study of Vesical Neck Obstructions, *Am. J. Roentgenol.* 62: 661 (Nov.) 1949.

3. Lower, W. E.: Trocar and Cannula for Suprapubic Drainage of Bladder, *Urol. & Cutan. Rev.* 2: 6 (Jan.) 1914. Engel, W. J.: Suprapubic Trocar Cystostomy: Evaluation and Presentation of an Improved Instrument, *Tr. Southeast. Sect. Am. Urol. Assn.* 14: 27, 1950.

incompatible with the diagnosis of prostatism. Fibrous contractures of the bladder neck commonly are the cause of very marked obstructive pathologic changes.

The treatment of patients having this silent mode of onset of prostatism is the same as in other cases of prostatic obstruction with severe vesical and upper urinary tract damage. As a general rule, drainage of the urinary tract is necessary until the kidney function has improved and stabilized and the patient's general physical condition permits prostatectomy with a reasonable chance of survival. If the obstruction has been discovered before serious renal injury has occurred, prostatectomy without preliminary drainage may be safe. My co-workers and I have tended to employ suprapubic drainage, usually the trocar type,³ performed under local anesthesia, in patients whose urine was uninfected but who had grossly distended bladders and serious damage of the upper urinary tract as judged either by the nonprotein nitrogen level or by intravenous urography. Prophylactic bilateral vasectomy is done at the time of cystostomy. It has often been possible with suprapubic trocar drainage to prevent the introduction of infection into the urinary tract at least until the renal function had improved considerably, and, in four of the eight patients who had initial suprapubic trocar drainage followed by prostatectomy two to three weeks later, the urine remained free of infection up to the time of the prostatectomy. With urethral catheter drainage, pyuria developed much more quickly despite careful technique and management.

With both urethral and suprapubic drainage the chronically distended bladder was emptied moderately slowly, usually by raising the inverted glass "Y" in the drainage tube to a height just permitting urine to flow over when the patient coughed or strained a little; this was lowered progressively over a two-day period until the "Y" was at the bladder level. Patients were not confined to bed unless an associated condition required recumbency. It is recognized that immediate, complete emptying of the bladder usually does no great harm, but in two of our patients whose distended bladders were rapidly emptied hematuria developed, with clots sufficient to interfere with drainage. Some such bleeding frequently occurs, but we had not seen this degree before. Since most of the patients in this group need prolonged drainage, we see no particular gain in sudden evacuation of the bladder and try to do it just slowly enough to avoid bleeding.

In addition to providing urinary drainage, efforts are made to improve the kidney function by supplying adequate fluids, to counteract the symptoms of acidosis by giving alkalis, to restore the normal hemoglobin by transfusion, and to correct nutritional and vitamin deficiencies. If infection is present, appropriate antibiotics and chemotherapy are employed as indicated and permitted by renal function. Prostatectomy is carried out when the blood nonprotein nitrogen level returns to normal or becomes stabilized, provided the patient's general physical condition allows any type of surgical procedure.

Of 14 patients in our group who came to operation, 7 had suprapubic enucleation of their prostates and

7 had transurethral resections. One patient who had suprapubic enucleation subsequently had transurethral resection of a greatly thickened vesical neck and prostatic capsule. Two patients were not operated on; one died of uremia three months after cystostomy drainage; the other is still being treated with suprapubic drainage, since he is in no condition for surgery one year after the establishment of this drainage. No operative deaths occurred in this group, but two men are known to have died five and six months, respectively, after operation, presumably of uremia; one had had a suprapubic, the other a transurethral, prostatectomy. It is our impression that those patients who had transurethral procedures had a somewhat easier, smoother postoperative course than the others, but the groups are too small for any significant comparisons. If the size of the prostate and other considerations permit, we favor the transurethral approach rather than an open surgical procedure on these and similar patients with impaired renal function.⁴ Attentive, prolonged preoperative and postoperative care must be provided regardless of the method of prostatectomy.

SUMMARY AND CONCLUSIONS

Attention is again called to the fact that prostatic obstruction may develop insidiously and pass unrecognized until serious, often irreversible, damage to bladder and kidneys has ensued. The significant findings in 16 such patients are reviewed; the mechanism of development, the diagnosis, and the principles of treatment are briefly discussed. Gastrointestinal complaints, symptoms of anemia, or the discovery of a suprapubic mass or seemingly very mild urinary disorders may bring these patients to the physician. The diagnosis of "silent" prostatism is not difficult if the condition is considered and the ordinary means of urologic study are employed.

605 Commonwealth Ave.

4. Greene, L. F., and Thompson, G. J.: Transurethral Prostatic Resection in Patients with Advanced Renal Insufficiency, *J. Urol.* 54: 166 (Aug.) 1945.

"Cancer Cures."— . . . Clinical trials of possible cancer cures in man are extremely difficult and fraught with pitfalls for the unwary. Since all the symptoms of cancer in man (apart from the presence of the tumour) are due to the secondary complications of sepsis, pressure, obstruction and hemorrhage, no improvement in the patients' general condition which does not include disappearance of the tumour can be admitted as evidence of specific action on cancer cells. Many substances, for example, lead (Blair Bell), lead selenide (Todd), bacterial products (Coley and others) and organic compounds of great variety, for example, colchicine, colchicine, nitrogen mustard et cetera, have been used in the past in clinical trials in man. Most of them appeared to produce temporary amelioration, but none has proved of any true value in the treatment of cancer. Early and complete surgical excision still offers the best hope, and in this connexion I must point out that even if a medical means of killing cancer cells specifically should ever be found there will still be immense scope for surgery. Relief of obstruction, mechanical restoration of function, "cosmetic" removal of a tumour mass and control of sepsis will all still be necessary, since cancer in the early stages is not painful and most often presents as an interference with function or as a visible tumour. The scope of a "medical" treatment would be an adjunct to this, to clear up any outlying cells or metastases.—W. E. Gye, *The Criteria of a Cancer Cure, Medical Journal of Australia*, Dec. 29, 1951.

"KREBIOZEN" IN TREATMENT OF CANCER

COMPARISON WITH OTHER THERAPY AS DETERMINED BY ENZYME ANALYSIS

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Since the exact chemical nature of "krebiozen" is unknown, the best way to determine its activity was to observe the physiological reactions caused by its administration. In order to analyze these reactions, Dr. William P. Phillips¹ requested that laboratory analyses similar to those being used to examine patients undergoing operations, radiation, or hormone therapy be carried out in the cases reported here. This study of patients being treated for cancer had been in progress for some time at Holy Cross Hospital Cancer Laboratory. In the study of physiological reactions to "krebiozen" Dr. Phillips administered the "krebiozen" and supervised the clinical course. Dr. James W. Henry² examined the biopsy specimens as well as surgical and autopsy material.

Investigators have confirmed that the antiproteolytic reaction of serum in man is increased in the presence of cancer.³ West and Hilliard⁴ demonstrated the proteolytic enzyme inhibitors of human blood in health and disease and their relation to neoplastic disease.⁵ West and associates used these same inhibitors to evaluate various therapeutic agents for cancer.⁶ This work clearly points to the delicate enzyme-antienzyme balance in man. Because therapeutic agents can modify the nitrogen kinetics in a tumor, their efficacy can be measured by determining the balance between the levels of the enzyme inhibitors for rennin and chymotrypsin. Quantitative laboratory methods for estimation of chymotrypsin and rennin inhibitors in human blood serum have been described,⁴ and the many factors other than malignancy that influence their concentration have been demonstrated. The adaptation of the balance of enzyme inhibitors for rennin and chymotrypsin to the course of a patient with proved cancer is demonstrated in several typical cases.

A positive diagnosis of cancer was made by biopsy for all patients in this study, including all patients who received "krebiozen." Enzyme inhibitor determinations were made by the technique of West and Hilliard⁴ at various intervals. Selected cases in which treatment was given with and without "krebiozen" are reported in detail.

The following data demonstrate that a careful study and interpretation of the serum concentrations of rennin and chymotrypsin inhibitors, correlated with sound clinical judgment, provide information about the activity of a proved cancer in a patient, and about the effects of the treatment for that cancer. The importance of this analysis is demonstrated by the multiple determinations shown in chart 7.

These enzyme-antienzyme balances are considered first in healthy persons, and then in relation to the effects of surgery, radiation, hormonal therapy, and "krebiozen" therapy on cancer and its course. Although several hundred determinations were made in many cases, only representative cases are presented.

NORMAL ENZYME INHIBITOR PATTERN

The normal value for rennin enzyme inhibitor is always moderately in excess of chymotrypsin inhibitor (chart 1). The level of inhibitor for chymotrypsin is considered normal when it is 5.5 units⁴ or less. At no time does the inhibitor for chymotrypsin measure quantitatively more than the inhibitor for rennin in the normal range. The balance remains constant week after week. Such activities as travel by air or automobile, long walks, long fasting, having a cold, or menstruation may produce slight deviation from the normal. Such temporary deviations, as well as one resulting from a major surgical procedure, will return to normal in a few days or weeks following recovery. The normal range for the inhibitor of rennin is between 7 and 12 units, and in a small percentage of cases, 20 to 50 units, especially in adolescents and children. In pregnancy, there is a steady increase of inhibitors for chymotrypsin above normal, but there is a corresponding rise of the inhibitors for rennin.⁷ The important finding is that the equilibrium between the two inhibitors is such that, at all ages, antirennin is normally in excess of antichymotrypsin.

RELATION OF ENZYME INHIBITOR PATTERNS TO ACTIVITY OF CANCER

A correlation has been observed between the enzyme inhibitor level of the serum and the rate of progress of malignant disease. Results obtained in a comparative study of two cases of carcinoma of the cervix are presented in detail.

CASE 1.—On March 8, 1951, M. G., age 39, noticed a considerable bloody discharge from the vagina. On March 29 she was hospitalized. Pelvic examination and diagnostic curettage

Virginia Pronske gave technical assistance in this study.

Clinical Instructor in Department of Surgery, Stritch School of Medicine, Loyola University; Director of Tumor Clinic and Cancer Laboratory, Holy Cross Hospital.

This work was supported by grants to the Dr. Donat Monaco Cancer Memorial Laboratory at Holy Cross Hospital from the National Ladies Auxiliary to the Veterans of Foreign Wars Cancer Research Fund.

1. St. Francis Hospital, Evanston, Ill.

2. Assistant Professor of Pathology, Stritch School of Medicine, Loyola University; Pathologist, St. Francis Hospital.

3. Clifton, E. E., and Young, L. E.: The Serum Antiproteolytic Reaction of Patients with Lesions of the Stomach and Duodenum, *Cancer* 3: 488-492, 1950. von Bergmann, and Meyer, K.: Über die klinische Bedeutung der Antitrypsinbestimmung im Blute, *Berl. klin. Wchnschr.* 45: 1673-1677, 1908. Brieger, L., and Trebing, J.: Über die antitryptische Kraft des menschlichen Bluts, *ibid.* 45: 1041-1044, 1908. Brieger, L., and Trebing, J.: Weitere Untersuchungen über die antitryptische Kraft des menschlichen Blutserums, insbesondere bei Krebskranken, *ibid.* 45: 1349-1351, 1908.

4. West, P. M., and Hilliard, J.: Proteolytic Enzyme Inhibitors of Human Serum in Health and Disease, *Proc. Soc. Exper. Biol. & Med.* 71: 169-172, 1949.

5. West, P. M., and Hilliard, J.: Proteolytic Enzyme Inhibitors of the Blood in Relation to Neoplastic Diseases: Preliminary Report, *Ann. West. Med. & Surg.* 3: 227-234, 1949.

6. (a) West, P. M.; Rapaport, S. I., and Tempereau, C. E.: Enzymatic Evaluation of Therapeutic Agents in Cancer, *Cancer* 4: 177-183, 1951; (b) Sensitivity of Serum Enzyme Inhibitors to a Variety of Cancer Chemotherapeutic Agents, *J. Clin. Invest.* 30: 547-557, 1951.

7. West, P. M.; Hilliard, J., and Mietus, A. C.: Serum Antiproteases in Normal Pregnancy: A Comparison with Changes Observed in Neoplastic Disease, *Surg., Gynec. & Obst.* 72: 209-212, 1951.

revealed an adenocarcinoma of the cervix. No treatment was instituted. Enzyme studies showed the pattern plotted in chart 2A.

CASE 2.—L. F., age 41, noticed a watery discharge from the vagina about May, 1951. In July she consulted her physician, who advised a biopsy. The biopsy revealed an adenocarcinoma of the cervix. Her enzyme inhibitor pattern is shown in chart 2B.

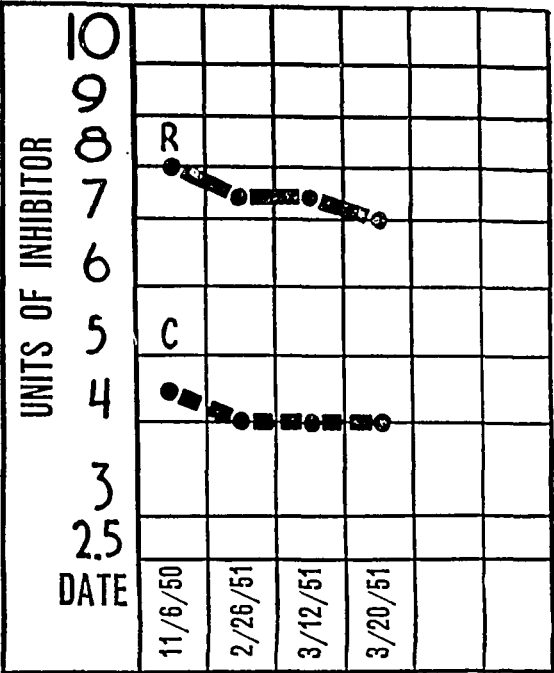


Chart 1.—Normal pattern of levels of rennin enzyme inhibitor and chymotrypsin enzyme inhibitor, determined at intervals in an adult with undisturbed metabolism from Nov. 6, 1950, to March 3, 1951. Single dash and dot line represents rennin inhibitor, and double dash and dot line represents chymotrypsin inhibitor.

Both patients appeared slightly ill. Weight loss was not too great, and their general subjective symptoms were about the same. Results of clinical examinations and the usual laboratory studies were similar for both. However, the enzyme inhibitor levels of the serum indicated a fundamental difference in the two patients.

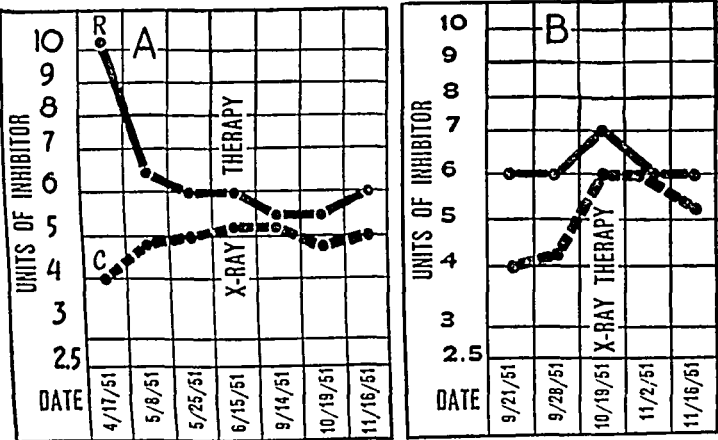


Chart 2 (cases 1 and 2).—Enzyme inhibitor levels showing correlation with progress of disease in two patients with adenocarcinoma of the cervix. In A, the pattern indicates slower growth of the tumor than in B. Single dash and dot line represents rennin inhibitor, and double dash and dot line represents chymotrypsin inhibitor.

M. G. (chart 2A) exhibited a pattern that is associated with rather slow growth. The level of rennin inhibitor was high at first, then gradually and steadily declined. The level of inhibitor for chymotrypsin gradually, but steadily, increased. In the case of L. F. (chart 2B), the level of enzyme inhibitor for chymotrypsin was low at

first and then rose rapidly, as seen in the third determination made on Oct. 19. A comparison shows that the tumor was more active in the case of L. F. than in the case of M. G., and that the rate of growth was greater in L. F. than in M. G.

EFFECT OF SURGICAL EXTIRPATION ON ENZYME BALANCE OF CANCER PATIENT

CASE 3.—In September, 1947, patient R. W. S. (chart 3) first noted a difficulty in reading fine print. In January, 1948, the glasses of the patient were changed, but the difficulty continued, and diminution of vision of the left eye was noted, with droop of the left lower eyelid. In August, 1949, loss of the sense of smell and marked congestion of the nose was noted. Loss of appetite and weight followed. In December, 1949, examination revealed a tumor in the left antrum, with obstruction of the left nasal passage, and bulging of the left eyeball was noted. The patient appeared gravely ill. X-ray examination was made, and biopsy revealed an adenocarcinoma of the antrum. Surgical and chemosurgical treatment was given, and on Dec. 24, 1949, further multiple microscopic examinations of the tissue revealed no tumor cells. The patient gradually but steadily improved, and has been well now for two years.

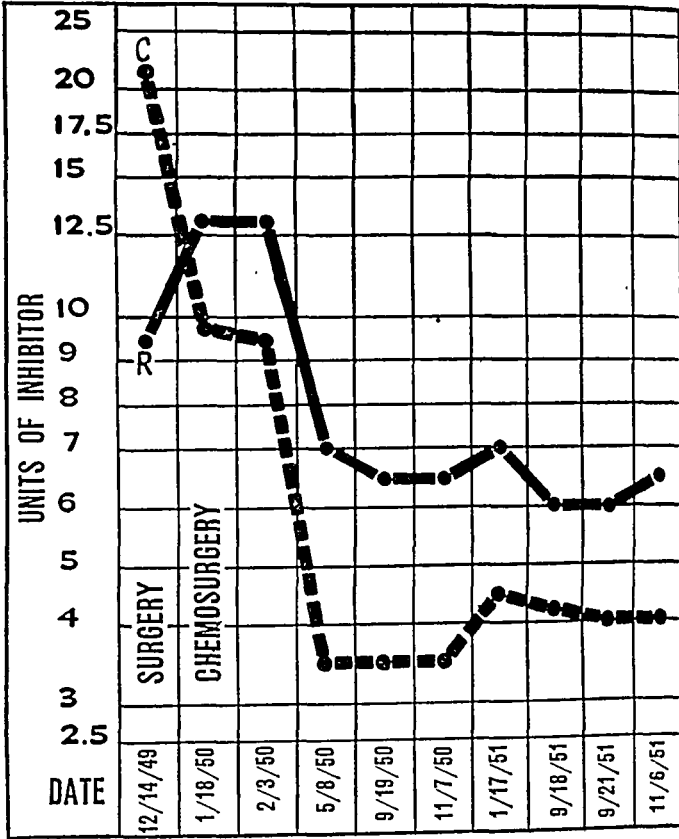


Chart 3 (case 3).—Effects of surgical and chemosurgical treatment on enzyme inhibitor levels of a patient with adenocarcinoma of the antrum. The surgical treatment was given on Dec. 14, 1949, and the chemosurgical treatment on Jan. 18, 1950. Single dash and dot line represents rennin inhibitor, and double dash and dot line represents chymotrypsin inhibitor.

Enzyme inhibitor balance determinations were made before surgical intervention and after treatment was completed. On Dec. 14, 1949, the imbalance was approaching the maximum. Following treatment further determinations were made. On Jan. 18, 1950, the enzyme imbalance began to improve markedly, indicating that the disturbing influence of the tumor was lessened. After the usual postoperative period, recovery was complete. Further enzyme determinations revealed that the balance of enzyme inhibitors was normal. The physiological effect of surgical extirpation that is illustrated has been demonstrated in many cases after surgery.

EFFECT OF X-RAY THERAPY ON ENZYME PATTERN OF CANCER PATIENT

The enzyme inhibitor patterns are highly sensitive and are an effective yardstick for the measurement of the effectiveness of radiation therapy in cancer also.

CASE 4.—S. S., a 41-year-old man, entered the hospital on Oct. 29, 1948, with the presenting complaint of swelling under the right arm of one year's duration. The patient stated that he had had the mass in the axilla for three years but had noted an increase in size for only the past year. No pain or diminished motion accompanied the tumor. The past history was not significant. The physical examination revealed no abnormality except a swelling in the right axilla, the size of a palm of the hand. The laboratory findings were within normal limits except for 4+ glycosuria. The fasting blood sugar level was 117 mg. per 100 cc. The day following admission a lipoma covering a mass of hard enlarged lymph nodes was discovered at operation. All the nodes and axillary fat were removed. Microscopic study revealed lymphogranulomatosis, Hodgkin's type, of the lymph nodes.

Enzyme inhibitor balance determinations were made following x-ray therapy. No other treatment had been administered before this x-ray therapy. At the first determination the disease was causing a high degree of imbalance and high rate of tumor metabolism (chart 4). Since

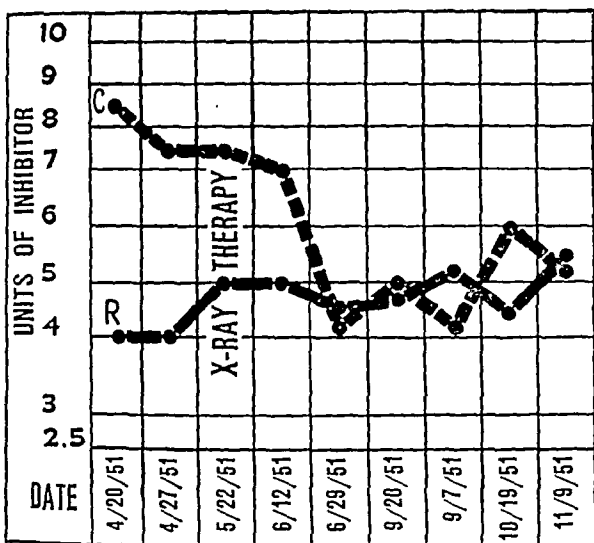


Chart 4 (case 4).—Improvement in balance of enzyme inhibitors following x-ray treatment on May 22, 1951, for Hodgkin's sarcoma. The single dash and dot line represents rennin inhibitor, and the double dash and dot line represents chymotrypsin inhibitor.

the first course of x-ray therapy was administered several months before the enzyme determinations were made, the effects of the treatment were no longer demonstrable. Further x-ray therapy was advised, and other enzyme determinations were made. On June 29, 1951, shortly following another course of x-ray therapy, the imbalance was shifted toward improvement, showing the beneficial effect of the treatment. Although the disease was active, the chart shows fairly good balance and the patient was progressing well clinically. The therapeutic effect of x-ray therapy is demonstrated by the pattern of enzyme inhibitor balance in this case.

EFFECTS OF HORMONE THERAPY IN CANCER AND INFLUENCE ON ENZYME INHIBITOR PATTERNS

CASE 5.—S. C., age 64, first noticed acute pain and a slight hematuria with marked difficulty in urinating on March 28, 1951. He was admitted to the hospital, and a cystotomy was performed on March 30. The patient's condition improved with

symptomatic and supportive treatment, and on April 17 transurethral resection of the prostate was performed. Histological examination revealed adenocarcinoma of the prostate. X-ray examination revealed metastatic lesions in the pelvis. Enzyme

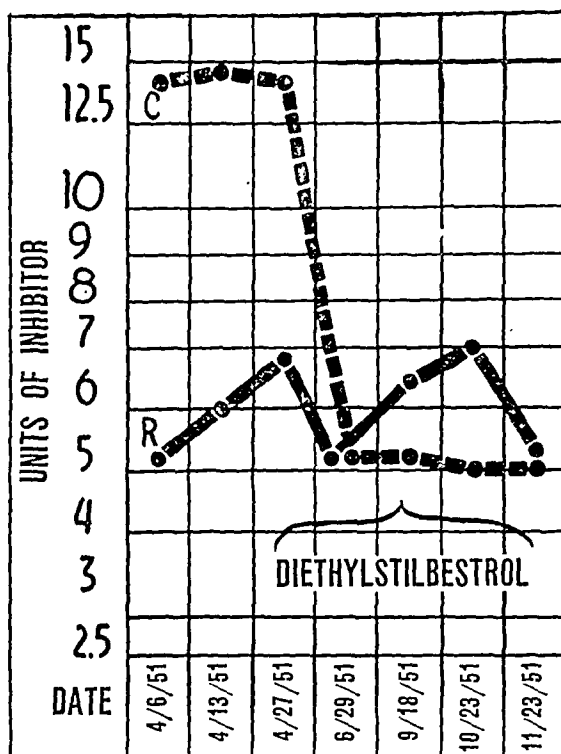


Chart 5 (case 5).—Improvement of enzyme inhibitor balance following administration of diethylstilbestrol from April 24 to Oct. 23, 1951, for cancer of the prostate. Single dot and dash line represents rennin inhibitor, double dash and dot line represents chymotrypsin inhibitor.

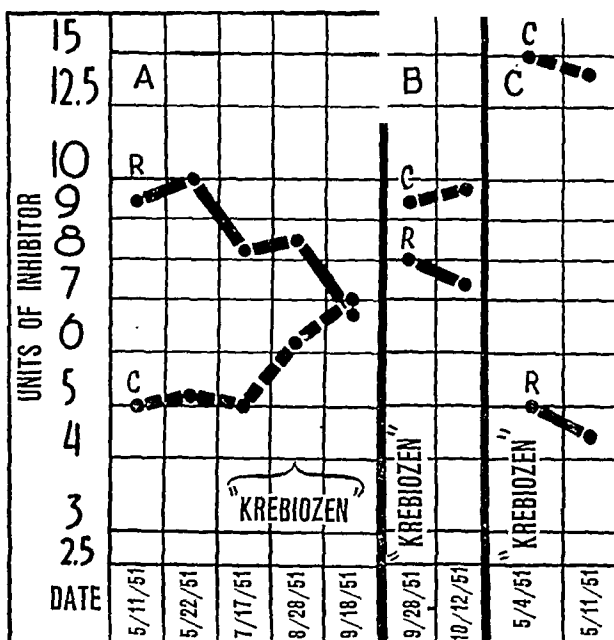


Chart 6.—Effects of "krebiozen" on enzyme inhibitor balance: A, in a patient with carcinoma of the lung who received the drug from May 22 until he died Oct. 19, 1951; B, in a patient with metastatic carcinoma of the bowel who received the drug on Sept. 28 and died Oct. 26, 1951; and C, in a patient with malignant melanoma who was given "krebiozen" on May 4 and died May 15, 1951. Single dot and dash line represents rennin inhibitor, double dash and dot line represents chymotrypsin inhibitor.

inhibitor levels were determined before diethylstilbestrol therapy was instituted and during therapy. The acid phosphatase value was 11.2 Bodansky units after cystotomy.

After transurethral resection and before hormonal therapy, the enzyme inhibitor levels for chymotrypsin and rennin were reversed, the level of inhibitor for chymotrypsin being quite high. It remained this way for about two months. On June 29 the level of the inhibitor for chymotrypsin dropped, and the patient improved subjectively (chart 5). Determinations made five and six months later showed continued improvement and control, although the disease was still active. The definite therapeutic effect is demonstrated on the chart, as well as the clinical improvement, which was so great that the patient returned to his daily routine and work. The acid phosphatase level on Nov. 19 was 6.1 Bodansky units. On Oct. 23 the hormonal therapy was stopped. Determinations one month later showed a decrease in the inhibition for rennin, revealing that the influence of diethylstilbestrol was weakened. Orchidectomy was planned.

EFFECT OF "KREBIOZEN" ON CANCER

There can be no doubt of the effectiveness of surgery, radiation, and hormonal therapy in treatment of cancer, as substantiated by these enzyme analyses. Many other drugs can be tested in a fairly short time for their effectiveness, as shown by West and associates.⁹ The drug called "krebiozen" was tested in 70 cases, 13 of which are incomplete, but 57 cases were thoroughly followed. Determinations of enzyme inhibition were made before, during, and after treatment with "krebiozen." Seven typical cases are presented in detail.

CASE 6.—In October, 1950, M. S., age 48, had a large bowel obstruction, and a large segment of the bowel was removed at St. Francis Hospital. The patient progressed well for four and one-half months. Gradually, abdominal pain with progressive abdominal enlargement developed. Paracentesis was performed, and large amounts of yellow fluid were removed. Another exploratory abdominal operation was performed on Feb. 10, 1951, and the diagnosis was metastatic cancer throughout the abdomen, with obstruction of the portal system. Following surgical recovery, three courses (1 cc. of "krebiozen" was given in each course) of "krebiozen" were administered. Determinations of enzyme inhibitor levels were made starting Sept. 28, 1951 (chart 6B).

Following initial treatment with "krebiozen," one course weekly was administered. There was no marked clinical improvement. The enzyme inhibitor levels were reversed from the start, and indicated progressive disease with a poor prognosis. The patient gradually declined and died on Oct. 26, 1951. In spite of intensive "krebiozen" administration, the patient's disease continued unaltered and finally destroyed the patient's life.

CASE 7.—In November, 1950, J. G., a 55-year-old man, had an upper respiratory infection. A roentgenograph of the chest revealed an area of consolidation in the upper lobe of the right lung that did not disappear or alter in appearance over a period of several weeks. The patient coughed violently on occasion, and once coughed up some tissue fragments that were examined microscopically. The examination revealed a carcinoma of the oat-cell type. "Krebiozen" therapy was instituted at the patient's request. He refused surgery.

Enzyme inhibitor studies were made before and during treatment with "krebiozen." Chart 6A shows that the tumor was present, but under natural control to some degree. In spite of intensive therapy with "krebiozen," the disease progressed and on Aug. 28, 1951, a marked increase in the metabolic rate of the tumor that disturbed the balance of enzyme inhibitors was noted. Clinically, the patient appeared more ill and began to look cachectic. On Sept. 18 further determinations showed greater progression of the disease, and on Oct. 19 the patient died following manifestations of a cerebral metastases.

In no instance in which a patient was treated with "krebiozen" was there any dramatic or startling change for the better. In the cases studied between April, 1951, and the present, 18 patients have died and all others show progressive disease. On the basis of ability to prognosticate the outcome at present, the outlook is very poor for those surviving. Aside from the laboratory analysis, clinical observation detected no unusual freedom from pain during treatment with "krebiozen." Such deadly cancer as malignant melanoma in one case progressed rapidly to death (chart 6C).

The relation of tumor metabolism to the balance of inhibitors of rennin and chymotrypsin is shown in chart 7. It shows the various patterns obtained in different cases with varied tumor activity. Although independently determined at Holy Cross Hospital Cancer

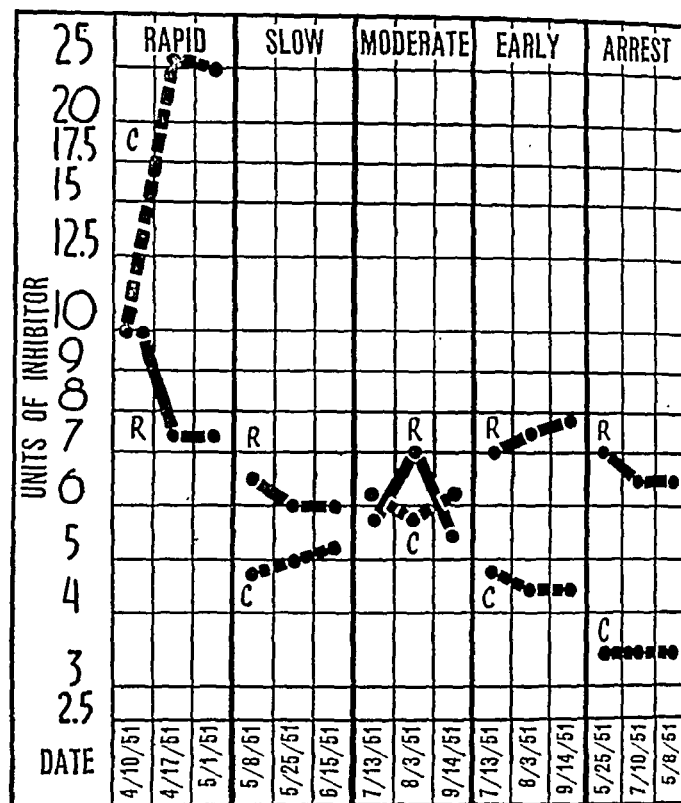


Chart 7.—Patterns of enzyme inhibitor levels correlated with tumor metabolism, as determined at the Holy Cross Hospital Cancer Laboratory.

Laboratory, these patterns are similar to those determined by West and Hilliard.⁸

The number and types of cancers among the 57 treated with "krebiozen" were as follows:

Cancer of larynx.....	1
Hypernephroma	1
Bowel carcinoma.....	10
Cancer of cervix uteri.....	8
Cancer of breast.....	16
Brain tumor (astrocytoma).....	1
Cancer of prostate.....	1
Cancer of stomach.....	1
Fibrosarcoma	1
Osteogenic sarcoma.....	2
Hodgkin's disease.....	1
Malignant melanoma.....	1
Lung carcinoma.....	4
Cancer of mouth.....	2
Cancer of tongue.....	1
Cancer of ovary.....	2
Cancer of skin and labia majora.....	4

In these cases 18 patients have died, and five autopsies have been performed. In addition 13 other cases of

8. Footnotes 4, 5, and 6b.

various types of tumors were studied, but insufficient observations were made on which to base firm conclusions.

The significant conclusion drawn from the study of patients treated for cancer with "krebiozen" and sufficiently followed is that in no single case has complete or partial inhibition of the cancerous growth been demonstrated. It is so completely ineffective that, whenever improvement in any case was suspected, it could easily be attributed to natural control or to other therapeutic agents used before "krebiozen" treatment was instituted. Growth of a cancer that could be described clinically as early was uninhibited by "krebiozen" and progressed to advanced stages.

Examination of the surgical and autopsy specimens of patients treated with "krebiozen" by Dr. James W. Henry revealed no significant change in cell structure or tumor architecture. The lymph node metastases were similar to their primary lesion. There were no significant findings microscopically that would indicate any phase of reticuloendothelial activity.

SUMMARY AND CONCLUSIONS

Enzyme inhibitor balances in human serum are useful in determining cancer cell activity of patients with a definitely proved cancer. This activity is measured in proportion to the impairment of the balance between the enzyme inhibitor for rennin and the enzyme inhibitor for chymotrypsin. Such a determination may indicate the quantity of cancer metabolism and quantity of physiological resistance. The greater the imbalance of the enzymes, the poorer the prognosis. If the balance is altered toward normal by a therapeutic agent, such an agent can be classified as effective if the beneficial effect can be repeated in a significant number of cases.

Surgical, radiation, and hormonal therapy have proved effective in altering cancer physiology. These agents correct the measurable imbalance in many cases and maintain a normal or near normal balance of the enzyme inhibitors significantly longer.

"Krebiozen" was one of the therapeutic agents used in this study, and was found to be ineffective. The West-Hilliard⁴ method of determining the level of enzyme inhibitors in human blood serum is a valuable guide in the management of the patient with cancer, and in evaluating therapeutic agents. The equilibrium between enzymes and the antienzymes of the blood serum is altered by a cancer in proportion to the efficacy of natural controls or to the stimulation or inhibition of these controls by other agents or complications.

55. E. Washington.

Chemically Induced Mutation of Cells.—As the physiology of the cell becomes better known, and the relation of chemical structure to cell and tissue is revealed, chemically induced mutation of cells may become possible. Certain hormones and other drugs are now known which affect the physical being as well as the mental attitude of an individual. The future may bring to us a series of drugs that will permit deliberate molding of a person, mentally and physically. When this day arrives the problems of control of such chemicals will be of concern to all. They would present dire potentialities in the hands of an unscrupulous dictator.—Roger Adams, *Man's Synthetic Future*, *Science*, Feb. 15, 1952.

CLINICAL NOTES

SEVERE OPTIC NEURITIS IN INFECTIOUS MONONUCLEOSIS

REPORT OF A CASE

Thomas W. Bonyng, M.D.

and

Karl O. Von Hagen, M.D., Los Angeles

The first case of central nervous system involvement in infectious mononucleosis in the American literature was reported by Epstein and Dameshek¹ in 1931. Subsequently only sporadic case reports appeared until 1940. Since then the number of reports has increased considerably, and it has been shown that this disease may involve several systems of the body and that the clinical course is greatly varied and utterly unpredictable. Thelander and Shaw² reviewed the cerebral complications, but did not mention papilloretinal edema or optic neuritis. Ashworth and Motto³ recorded a case of infectious mononucleosis complicated by bilateral papilloretinal edema with no evidence of meningitis or encephalitis. Blaustein and Caccavo⁴ described a case complicated by bilateral papilloretinal edema. Piel and his co-workers⁵ reported a case of infectious mononucleosis involving the central nervous system with bilateral papilledema that resulted in slight visual difficulty. Severe visual impairment never was noted to result from optic neuritis or papilloretinal edema. Accordingly, we are reporting a case of infectious mononucleosis in which marked visual impairment was the presenting complaint and moderately severe optic neuritis was the only prominent finding.

REPORT OF A CASE

S. P., a 14-year-old white girl, was examined on May 16 because of progressive severe dimness and blurring of vision of two weeks' duration. She had been perfectly well until April 29, when frontal headaches developed that persisted for several days. She had coryza and a slight elevation of temperature for a few days beginning May 1 and consequently remained home from school for two days. On May 6 and 7 she made a trip to the mountains; on her return she was excessively fatigued and her eyes felt swollen. A school nurse observed on May 8 that the patient's eyelids were swollen and that she had a slight elevation of temperature, and accordingly sent her home. The following day blurring of vision developed, her throat was slightly sore, and her temperature was 101 F. She also had difficulty initiating her urinary stream. Her visual acuity decreased rapidly from May 9 to 12, so that she could hardly identify even close relatives and could scarcely differentiate colors. She received penicillin parenterally for three days, but the low-grade fever, malaise, anorexia, lethargy, asthenia, and marked

1. Epstein, S. H., and Dameshek, W.: Involvement of Central Nervous System in Case of Glandular Fever, *New England J. Med.* **205**: 1238-1241 (Dec. 24) 1931.

2. Thelander, H. E., and Shaw, E. B.: Infectious Mononucleosis, with Special Reference to Cerebral Complications, *Am. J. Dis. Child.* **61**: 1131-1145 (June) 1941.

3. Ashworth, J., and Motto, S. A.: Infectious Mononucleosis Complicated by Bilateral Papilloretinal Edema: Report of Case, *New England J. Med.* **237**: 544-545 (Oct. 9) 1947.

4. Blaustein, A., and Caccavo, A.: Infectious Mononucleosis Complicated by Bilateral Papilloretinal Edema: Report of Case, *Arch. Ophthalmol.* **43**: 853-856 (May) 1950.

5. Piel, J. J.; Thelander, H. E., and Shaw, E. B.: Infectious Mononucleosis of Central Nervous System with Bilateral Papilledema, *J. Pediatr.* **37**: 661-665 (Oct.) 1950.

visual impairment persisted, so she was admitted to the Hospital of the Good Samaritan on May 16.

Physical examination revealed a fairly well-developed and well-nourished, apathetic and lethargic girl. Her blood pressure was 110/68, and the pulse rate was regular at 88. She was barely able to count fingers with either eye. There was an unusual staring appearance, with limitation of ocular excursions in nearly all fields, and a cover test revealed 8 D. hyperphoria in the left eye. There was no diplopia. The pupils were markedly dilated and reacted sluggishly to light. The fundi showed edema and hemorrhagic reaction involving the optic nerves bilaterally, with obliteration of disk margins on the right, splinter hemorrhages in the area adjacent to the disks, and moderate venous engorgement. There was slight pain on motion of the eyes and tenderness to palpation. The visual fields showed large central scotomas and some peripheral constriction. The neck was not rigid. A few lymph nodes 0.5 to 1.0 cm. in diameter were noted in the right occipital, posterior cervical, axillary, and inguinal regions. The pharynx was normal. The spleen was palpated 2 cm. below the left costal margin and was slightly tender and firm. Neurological examination showed no motor weakness or ataxia. All the tendon reflexes were equal and within normal limits. The Babinski sign was equivocal on the right. Abdominal reflexes were absent. Sensation was intact everywhere.

On May 17 the hemoglobin level was 13.7 gm. per 100 cc. The erythrocyte count was 4,600,000 and the leukocyte count 8,000, with 22% polymorphonuclear cells, 2% basophilic cells, 3% monocytes, and 73% lymphocytes. Many of the cells were typical of infectious mononucleosis. A Wassermann reaction and result of a Kahn test were negative. On May 18 blood studies showed the differential heterophil antibody (Davidsohn) test to be positive. The presumptive test with the patient's serum versus sheep cells showed agglutination of the cells in serum dilutions from 1:7 to 1:1,792. The differential tests with the patient's serum absorbed with guinea pig antigen showed agglutination of cells in serum dilutions from 1:7 to 1:896. On May 17 a spinal fluid examination revealed a cell count of six leukocytes per cubic millimeter. The protein level was 55 mg. per 100 cc., and the result of a Kolmer test was negative. The colloidal gold curve was 1112321100. A diagnosis of infectious mononucleosis was made, and on May 18 intensive aureomycin therapy (250 mg. every two hours) was initiated and continued for five days.

Furmanski⁶ reported on the use of dimercaprol injection (BAL) in treatment of severe peripheral neuropathies. He presented the theory of some neurologists that neuropathies are initially biochemical disorders of the neuron, due chiefly to disruption of one or more enzyme systems that regulate the metabolism of the cell. According to this hypothesis, the resulting neuronal dysfunction can be severe, but structural changes in the myelin or axon need not occur. Neurons in this stage of dysfunction should be able to recover rapidly over a period of hours or days if enzymatic equilibrium is restored. He mentioned that J. M. Nielsen, senior consultant in neurology at the Birmingham Veterans Administration Hospital, had suggested that neuropathies be treated by attempts to restore enzymatic equilibrium with the substance that had demonstrated such ability in heavy metal intoxications, namely, dimercaprol injection. Accordingly, such treatment was instituted by Furmanski in four cases, with excellent results in three and improvement in one.

Creaturo⁷ subsequently reported a case of infectious mononucleosis with polyneuritis in which facial paresis

and diplegia were prominent findings. During convalescence the paresis of the legs became static, and it was decided to employ dimercaprol injection in the dosage recommended by Furmanski. During a period of 13 days 1.125 gm. were administered, and remarkable improvement occurred, apparently as a result of the therapy with dimercaprol injection.

Because of the possibility that dimercaprol injection might have a beneficial effect on cranial nerve neuropathy of toxic origin, we instituted such treatment in our patient, who still had marked visual impairment, with the hope that normal vision might be restored.

It is impossible to evaluate accurately the efficacy of dimercaprol injection in this particular instance because the patient's sight was slowly improving when dimercaprol therapy was started. However, close observation seemed to reveal pronounced, rapid improvement in visual acuity 12 to 24 hours after administration of dimercaprol. This tendency continued during the seven days of dimercaprol therapy, so that the patient was able to read $\frac{1}{8}$ in. (0.32 cm.) print at 3 ft. (91.4 cm.) when the drug was discontinued. The total dosage was 700 mg. administered over seven days. Her vision subsequently continued to improve, but objects persistently appeared fuzzy and color differentiation was still impaired six weeks after the onset of this illness. Only trivial visual symptoms were noted 10 weeks after onset, and examination by an ophthalmologist 12 weeks after the onset revealed 20/20 vision in each eye, some optic atrophy, normal visual fields, and normal color perception.

Bower⁸ for several years has used gamma globulin in the treatment of severe cases of infectious mononucleosis. His results have been very good, rapid therapeutic response being manifested within 24 to 48 hours. He is very enthusiastic and advocates the use of this form of therapy even in milder cases.

Fortunately, in many instances secondary optic neuritis regresses, with no permanent residual visual impairment. However, there is always the possibility that permanent visual impairment will result in certain cases of optic neuritis. Unfortunately, the present trend toward bizarre manifestations in infectious mononucleosis seems to indicate that increasing numbers and even severer cases of optic neuritis of this type will be seen in the future.

Accordingly, we feel it is advisable in all cases of infectious mononucleosis to be alert to the possibility of peripheral or central nervous system involvement, so that treatment with dimercaprol injection and/or gamma globulin can be instituted as early as possible.

SUMMARY

A case is reported in which infectious mononucleosis was complicated by involvement of the central nervous system, causing optic neuritis with severe visual impairment. Recovery was complete. Unusual neurological complications may occur in this disease. Dimercaprol injection (BAL) has been used with apparent success in treatment of peripheral neuropathies, and was employed in this instance with suggestively encouraging results. Both gamma globulin and dimercaprol injection may be beneficial in treatment of infectious mononucleosis.

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SUICIDE ATTEMPT WITH WARFARIN, A BISHYDROXYCOUMARIN-LIKE RODENTICIDE

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Through the ages the rat, which has caused untold amounts of sickness and death as well as property damage that far exceeds human imagination, has been a major scourge of mankind. Investigators throughout the world have searched for the ideal rat poison, which, according to O'Connor,¹ must have the following characteristics: 1. It must be surely effective in baits of small quantity so that its presence is not detected by the rodent. 2. The finished bait must not excite shyness of the rat population so that the necessity for prebaiting is avoided. 3. The manner of death must be such that surviving rats will not become suspicious and will remain on the premises eating of the bait until they, too, die. 4. The poison must be species specific unless its use can be made safe for man and domestic animals by some other means.

This ideal rodenticide proved to be very elusive until Link and his associates² published their papers on the hemorrhagic sweet clover disease of cattle. This work led to the use of antiproteolytic anticoagulants, e. g., bishydroxycoumarin (dicumarol®), as preventives of intravascular clotting and thrombosis in treatment of various human diseases. Their work stimulated research into the possibility and feasibility of using these anticoagulants in extermination of rodents. From this research came the drug warfarin, which Link named for the Wisconsin Alumni Research Foundation; warfarin is also known as compound 42 and WARF-42. There are several trade name formulations, including "dethmor," "rax powder," and "d-con."³

Warfarin toxicity and effectiveness have been thoroughly studied on various laboratory animals by Link and his group at the University of Wisconsin and on rats in the field by Hayes and Gaines⁴ and Schein.⁵ It has proved to be a very effective rodenticide and has been considered relatively safe for domestic animals and humans. In order to cause toxication it must be given in one very large dose or in repeated small doses over four to six days. No cases of poisoning in man have been reported to date.⁶ In view of the foregoing facts, we feel it is worthwhile to report the findings and treatment of the first case of warfarin poisoning in a human in hope that it will alert the medical profession to the diagnosis and management of future cases.

E. J. H., a 22-year-old, white Army inductee, was admitted to the Medical Service of the United States Naval Hospital the evening of April 4, 1951. He stated that, because he had been depressed concerning induction into the service, he had attempted suicide by taking "d-con," a form of rat poison. On the night of March 26 the patient had taken a small portion of the poison orally in the form of dry powder. He stated that it tasted somewhat sweet, like marshmallow, and that the poison had caused no unpleasant sensations in the mouth or stomach. He had continued to take about equal amounts daily through March 31 and had consumed a 4 oz. (113 gm.) carton in those six days. The patient stated that he took the poison in this manner because he failed to obtain the anticipated results with any single dose.

He noticed no ill effects of the drug until 48 hours before admission, when he began to have back pain in the region of the kidneys and abdominal pain that was generalized but not severe. The pains continued until admission, and he experienced one episode of vomiting the day prior to admission. Furthermore, on the day before admission he had intermittent epistaxes. His nose would bleed for 15 to 20 minutes at a time, especially if he lay down, and the epistaxis would be followed by a nasal discharge of pinkish fluid. The patient denied the presence of any blood in his urine or in the vomitus. He had had no bowel movements since he had taken the first dose of "d-con."

The psychiatric component of this patient's history is not included, because it has no bearing on the purpose of this report. The remainder of the history revealed no abnormalities and the patient had been perfectly healthy prior to taking the poison.

Physical examination on admission revealed a well-developed, well-nourished young white man who appeared acutely ill; furthermore, he was obviously mentally depressed. He did not care to elaborate about his symptoms, but he did answer all questions clearly and intelligently. His temperature was 98.6 F, pulse rate 130, respiration rate 24, and blood pressure 160/100. There was a petechial rash over the shoulders, anterolateral chest walls, medial surfaces of the arms, axillae, abdomen, and inner thighs; in addition, a few petechiae were noted over the back. The conjunctivas were slightly injected, and the pupils were dilated and reacted to light and accommodation. Ophthalmoscopic examination revealed no retinal hemorrhage. There was a brownish-red discharge coming from both nostrils, and the mucous membranes were very hyperemic, but no active bleeding points were discernible. There was no bleeding from the gums. There was no lymphadenopathy. The lungs were clear. A grade 1 systolic, nontransmitted murmur was heard over the apical region. The abdomen was flat and quite tender throughout, especially in the left lower quadrant. There was no definite rebound tenderness, but the abdomen was semirigid. No viscera or masses were palpable. Rectal examination revealed normal brown-colored feces without gross evidence of blood. There was slight bilateral costovertebral angle tenderness to fist percussion. No signs of neurological involvement were evident.

The patient, when questioned concerning the contents of "d-con," said, "It had dicumarol® on the label." It was later learned during a psychiatric interview that the patient had learned of this compound from a recent issue of a popular magazine. J. C. Munch⁷ verified that the active ingredient of "d-con" was warfarin.

On admission the laboratory findings revealed a white blood cell count of 13,700, with 72% segmented polymorphonuclear leukocytes, 3% band form cells, 17% lymphocytes, 7% monocytes, and 1% basophil cells. The hemoglobin value was 13 gm. per 100 ml. The patient's prothrombin time was 4 minutes 6 seconds compared to a control time of 15 seconds. The Lee-

The opinions or assertions contained herein are those of the authors and are not to be construed as reflecting the views of the Navy Department or the naval service at large.

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White coagulation time was 35 minutes; the clotting time by the capillary tube method was 9 minutes; and the bleeding time was 2 minutes. The blood calcium level was 10.7 mg. per 100 ml. The urinalysis revealed a specific gravity of 1.015, a trace of albumin, and many red blood cells per high power field.

The laboratory evidence of marked hypoprothrombinemia established the diagnosis of warfarin poisoning. The patient was then transfused with 500 ml. of fresh whole blood and given 72 mg. of vitamin K intravenously. On the morning of April 5 the patient's symptoms and signs remained unchanged. The patient had a normal bowel movement with no evidence of blood. Laboratory findings included a prothrombin time of 54 seconds compared to a control of 14 seconds, or 4% of normal, a white blood cell count of 9,400, with a normal differential count, a hemoglobin value of 14.7 gm. per 100 ml., a hematocrit level of 47 vol. of packed red cells, and a red blood cell count of 6,500,000. The Lee-White coagulation time was 58 minutes. The bleeding time was two minutes. Urinalysis revealed an acid urine of 1.016 specific gravity, 1+ albuminuria, and many red blood cells. On this day he was also given a transfusion of 500 ml. of fresh whole blood, and a total of 144 mg. of vitamin K was administered intravenously in two equally divided doses 12 hours apart.

On April 6 the signs and symptoms were essentially unchanged. No new petechiae were noted. The patient had a normal-colored bowel movement followed by a passage of gross blood. The laboratory findings revealed a hemoglobin value of 13 gm. per 100 cc., a prothrombin time of 37 seconds compared to a control time of 14 seconds, or 12% of normal, a Lee-White coagulation time of 28 minutes 10 seconds, and a blood urea nitrogen level of 12.2 mg. per 100 ml. The urinalysis revealed a grossly bloody, acid urine with 1.017 specific gravity and 2+ albuminuria. He was again given 144 mg. of vitamin K intravenously in two equal increments. With the appearance of blood in the urine the patient was given sodium bicarbonate in an effort to alkalinize the urine. The urinary output the first two days exceeded 1,000 ml. daily, and this rate of output continued throughout the entire period of observation.

By April 7 the patient's abdominal pain and back pain were almost gone and were described as a "soreness." His blood pressure was 140/95. The petechiae were still present, but no new ones could be found. His bowel movement was of normal brown color and contained no gross blood. The patient's prothrombin time was 24 seconds compared to a control time of 14 seconds, or 27% of normal. The urine was still bloody, but alkaline in reaction, and contained albumin (4+). He was given mg. of vitamin K intravenously in two doses, and he was again transfused with 500 ml. of fresh whole blood.

On April 8 the patient was asymptomatic except for a temperature of 100.6 F in the morning, which subsided during the day. The blood pressure returned to a normal level of 120/75. The prothrombin time was 20 seconds compared to a control time of 14 seconds, or 37% of normal. The Lee-White coagulation time was 11 minutes. Bleeding time was 1 minute 20 seconds. The urine remained grossly bloody. The patient was again given 20 mg. of vitamin K intravenously.

The patient's rash began to fade on April 9 and was gone by April 13. The prothrombin times for April 9, 10, and 11 were respectively 16 seconds or 60% of normal, 15 seconds or 70% of normal, and 14 seconds or 100% of normal. The urine of April 9 was a clear straw color, and a rare red blood cell was seen microscopically. Results of subsequent urinalyses were completely normal. During these last three days of observation the patient received 20 mg. of vitamin K intravenously daily. During the entire illness the patient had no symptoms except those present on admission, and he was completely comfortable without sedation.

COMMENT

Chemically warfarin is 3(α -acetylbenzyl)-4-hydroxycoumarin. It is a colorless, odorless, and practically tasteless compound. The action of the drug is almost identical with that of bishydroxycoumarin in that it

inhibits the formation of prothrombin by the liver. Its capacity to produce hypoprothrombinemia is, however, some 40 times that of bishydroxycoumarin. The rationale of the use of warfarin as a rodenticide is to cause fatal internal hemorrhages. The rodent must consume a portion of the bait in which the warfarin is mixed daily for four to six days in order for death to occur. The amount of the drug necessary to produce these results when taken in this manner is 1 mg. per kilogram of body weight. The fact that the chemical does not cause bait shyness has made it very acceptable as a rodenticide, and it approximates the ideal rat poison according to the aforementioned criteria.

Warfarin is distributed to commercial firms in a 1:200 mixture with cornstarch. The finished bait is then prepared by adding a grain, usually corn meal, which the rat prefers. It contains warfarin in 1:4,000 concentration by weight. "D-con," which is a commercial rat poison advertised on a nationwide basis, contains warfarin and lures, the latter being one of a group of vegetable oils of which the rat is very fond. It is packaged in two forms, the concentrate and the ready bait. The patient took the concentrated form, 4 oz. (113 gm.) of which contained 567 mg. of warfarin.⁸

The danger to domestic animals, especially cats and dogs, depends on the possibility of their taking some of the drug daily for several days. When the poison is placed in properly constructed bait shelters, this danger should be minimized. However, if the animals were to eat dead or sick rats for several consecutive days, they could develop toxic manifestations and die. Link, however, has shown that secondary poisoning depends largely on the warfarin remaining in the alimentary tract of the poisoned rats, and not on the concentration of warfarin in the tissues of these rodents. Chickens are very unlikely to be affected, although they are the most likely of barnyard animals to eat the bait. Their "immunity" seems to be conferred by their habit of pecking in the dung of the animals in the area. It has been shown that the concentration of vitamin K is quite high in the feces of the common barnyard animals.⁸ The vitamin K thus protects against the action of ingested warfarin.

The danger to humans is obviously quite small. Link and others have shown that a single dose of the drug, even if large, is unlikely to depress the prothrombin time to the critical level. However, one large dose has caused hemorrhagic manifestations in pregnant laboratory animals. The possibility of accidental poisoning of children is minimal, even if the bait is inadvertently left in available locations. Accidental poisoning of an adult is almost inconceivable. Taking the drug for suicidal purposes would require marked perseverance and a continued desire, lasting over several days, to die. These factors plus the repeated use of the drug in an effort to get the drastic results expected of rat poison, such as those known to occur when poisons containing phosphorous, arsenic, alpha-naphthylthiourea, or fluorides are used, would result, as they did in this case, in a full-blown clinical picture of warfarin toxication. The drug is to be recommended as a rodenticide, not only for the above reasons, but also because, if accidental or intentional

8. Segard, C. P.: Personal communication to the authors.

poisoning does occur, the toxic manifestations can be treated by giving vitamin K and fresh whole blood.

It is felt that the treatment of warfarin toxication is more likely to be successful than the treatment of poisoning due to other common rodenticides. The delay in the decrease of prothrombin in the blood following the initial dose and the presence of vitamin K in the normal diet are factors that increase the likelihood of successful therapy. The treatment of bishydroxycoumarin toxication has been common knowledge to the medical profession for several years, and, since warfarin toxication is essentially the same, the treatment will not be detailed any further. The inadequacies of the present treatment of bishydroxycoumarin toxication are well known, and it is hoped that more effective antidotes will be forthcoming. If there is urinary bleeding, then it seems wise to alter the pH of the urine to the basic side in order to lessen the likelihood of precipitation of acid hematin in the renal tubules, which, in sufficient amounts, could cause anuria, uremia, and death.

SUMMARY

A proved case of human poisoning due to warfarin, a relatively new rodenticide which has an antiprothrombin action similar to that of bishydroxycoumarin (dicumarol®), has been presented. The relationship of warfarin to bishydroxycoumarin has been delineated, and the pathological physiology of this form of poisoning and the measures employed to correct these abnormalities have been discussed.

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EXACTING CONSERVATIVE MANAGEMENT OF THE GANGRENOUS TOE

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In an extremity supplied by arteriosclerotic vessels, the most distal parts will be subject to tissue changes should the peripheral circulation be in any way further impaired. In a case of arteriosclerosis, with no palpable blood vessel pulsation, and with oscillometric readings of zero, the presence of a gangrenous toe or a portion thereof does not necessarily indicate that the circulation of the extremity is such as to require amputation of any portion of the extremity except the involved local part.

Spontaneous gangrene of the toe is extremely rare if it ever occurs. Such a condition would imply that the circulation to the toe for some unexplainable reason was suddenly stopped. On the contrary, in nearly every case of gangrene of the toe some history of trauma can be elicited, even though the trauma may have been so minor as to have been practically unnoticed by the patient. All trauma to tissues, whether by infection, temperature changes, chemicals, or lacerations, results in edema of varying degree. It is not unreasonable to assume that in a toe in which the circulation is already precarious, any such edema may easily obstruct this impaired circulation. It is this edema, even though very slight, which immediately precipitates the devitalization of the tissues, with resultant gangrene; even the surgeon's sharp scalpel can produce gangrene on this basis. Gangrene of the nail-

bed following removal of a toe nail in such patients is explained on similar principles.

This report will not deal with therapeutic measures other than those immediately concerned with the toe. The general needs of the patient are taken for granted. Vasodilating drugs and sympathetic block may be useful at times. After some trial, I have not been impressed with the reported claims of tocopherol. The use of heat in any form cannot be too strongly decried. Heat increases the metabolism of tissues, which, in turn, require more blood supply. The impaired vessels cannot furnish the increased tissue needs; hence the tissues must suffer additional damage. On the contrary, since it would appear preferable to cool the tissues and thus lower their metabolism, I cover the toe with a light gauze dressing, which is kept continually moist with 70% alcohol. This not only tends to keep the part clean but, by its constant evaporation, produces some cooling effect. The foot is never placed under bedcovers but is exposed to room temperature to aid evaporation. When the gangrenous portion has become well demarcated and somewhat shriveled, it will also shrink at its junction with the vital part of the toe, leaving a circular indentation, which identifies the place at which the amputation should be performed. With sterile surgical scissors, the toe is clipped exactly at this point of demarcation. A scissors is advised since with this instrument the surgeon will be less likely to cut into the nongangrenous tissues as he might do with the scalpel. If the amputation is performed more proximal, even by as much as a few millimeters, the tissues respond to this trauma by increased edema, resulting in further gangrene. This phenomenon probably explains the appearance of gangrene with each new low amputation, which previously discouraged these amputations and led to the advocacy of high amputations. No anesthesia is ever necessary for the "scissors amputation" here described. The alcohol dressing is continued, and the moistening of this can very well be done by the patient. Antibiotics are absolutely essential, and treatment with them must be continued until the toe end is on its way to healing. I have used only penicillin. The patient is advised to elevate the leg as much as possible, but absolute bedrest is unnecessary.

The results with such management have been encouragingly good, even with extremities in which no arterial pulsations were discernible and in which oscillometric readings were zero. Occasionally, it will be noted that after some time in such cases, without any other therapy, some oscillometric readings will be obtained. Possibly, in such cases, a reflex vascular spasm due to the local pathology has existed. It is therefore suggested that the condition in such cases may be improved with the use of vasodilating drugs and sympathetic block. Most important, however, is the necessity of avoiding heat, of keeping the part clean and preventing infection, and of amputating the toe at exactly the correct level. This constitutes what may be designated as "exacting conservative management," which, it is believed, will result in saving limbs that might otherwise be amputated.

ACUTE MORPHINE POISONING WITH
MANIFESTATIONS OF PANCREATITIS

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Although acute morphine poisoning is not uncommon, as Tovell points out,¹ the American literature contains few reports of this condition in contrast to the numerous articles that have appeared on chronic morphine intoxication or addiction. The present case is of interest because the patient recovered from an unusually large dose of morphine given intravenously and because of certain clinical manifestations that were noted.

REPORT OF A CASE

A 19-year-old student nurse was found comatose and cyanotic, with no discernible respiratory movements. Artificial respiration (manual) was begun immediately. It was noted that the pupils were miotic and that there was a fresh venipuncture wound in the left antecubital fossa. A quick search revealed a syringe

was given 600,000 units of procaine penicillin and 1 gm. of streptomycin intramuscularly twice daily.

After 12 hours, respirations were 12 per minute and the patient was easily aroused, although she drifted off to sleep when left alone. Pupils were still pinpoint and nonreactive. The abdomen was noted to be slightly rigid, and she winced when the epigastrium was palpated. A short time later, she began to complain bitterly of epigastric pain with radiation to the back. She became nauseated and vomited small amounts of coffee-ground material; this later became mucoid with streaks of bright red blood. Epigastric tenderness without rebound pain persisted. A serum amylase determination was performed 30 hours after the injection of the morphine and was found to be 815 units (normal 50 to 150 units). She was given glucose and isotonic sodium chloride solution, and the nausea was controlled with atropine and phenobarbital sodium. During the next 48 hours there was gradual subsidence of pain and nausea, and the serum amylase activity 72 hours after morphine injection was only 99 units. She became alert on the second day and for about 12 hours complained of generalized pruritus. Inability to urinate necessitated catheterization for two days. The miosis persisted for 48 hours, normal pupillary reactivity to light reappearing on the third day. She became afebrile on the fourth day and began to take a liquid diet, and recovery proceeded rapidly. Moderate constipation was successfully relieved by enemas. There was no evi-

Summary of Reported Cases of Acute Morphine Poisoning with Recovery

Drug, Dose	Route	Reference
Morphine acetate, 1.0 gm.....	Oral	Tardieu, A.: Die Vergiftungen in gerichts-arztlicher und klinischer Beziehung, Erlangen, Ferdinand Enke, 1893, p. 504
Morphine sulfate, 4.025 gm.....	Oral	Reese, J. J.: Manual of Toxicology, Philadelphia, J. B. Lippincott Company, 1874, p. 373
Morphine hydrochloride, 1.0 gm.....	Oral	Holst, V.: St. Petersburg. med. Wchnschr. 7: 421, 1892
Morphine hydrochloride, 3.0 gm.....	Oral	Nothnagel: Allg. Wien. med. Ztg. 29: 368, 1894
Morphine hydrochloride, 2.0 gm.....	Oral	Playfair, D. T.: Lancet, 2: 545, 1893
Morphine hydrochloride, 0.9 gm., plus barbitol sodium, 5 gm...	Oral	Godde: Deutsche med. Wchnschr. 7: 204, 1917
Morphine hydrochloride, 1.7 gm., plus barbitol sodium, 5 gm...	Oral	Rautenberg, E.: Deutsche med. Wchnschr. 45: 1277, 1919
Morphine hydrochloride, 1.5 gm.....	Oral	Joachimoglu, G.: Deutsche med. Wchnschr. 45: 1413, 1919
Morphine hydrochloride, 3.6 gm.....	Oral	Stern, S.: Deutsche med. Wchnschr. 51: 316, 1925
Morphine sulfate, 0.4 gm.....	Subcutaneous	Tovell, R. M.: Proc. Staff Meet., Mayo Clin. 8: 616, 1933

containing a small amount of clotted blood and three empty morphine sulfate solution vials. According to the ward narcotics record and the story later obtained from the patient, she had ingested 0.76 gm. (approximately 12 grains) of morphine sulfate intravenously in a suicide attempt. The pulse rate was 120 and blood pressure 104/70. The skin was cyanotic and cold, and she was sweating profusely. There was no detectable respiratory activity. The pupils were miotic and nonreactive to light. All reflexes, including the corneals, were absent, and she was completely unresponsive to external stimuli. An endotracheal tube was inserted, and 100% oxygen was administered under positive pressure, with rapid disappearance of cyanosis, but the patient made no spontaneous respiratory movement for about one hour. Carbon dioxide was not given with the oxygen. An intravenous infusion of 5% glucose in isotonic sodium chloride solution was started in order to facilitate the intravenous administration of stimulants. During the first six hours of treatment, the patient received a total of 12 gm. of nikethamide (coramine®), 4 gm. of caffeine and sodium benzoate, and 40 mg. of amphetamine intravenously. Thereafter she was given 0.5 gm. of caffeine and sodium benzoate subcutaneously at three to four-hour intervals for two days.

After six hours, respirations were 6 to 8 per minute, the pulse had slowed to 92 to 96 per minute, and the patient would respond to her name. Rectal temperature had risen to 101 F. The endotracheal tube was removed, and oxygen was administered by nasal catheter for the next 24 hours. Because of the fever and the appearance of numerous rhonchi throughout both lungs, she

dence of any residual mental or neurologic change and no further abdominal difficulty. She was discharged on the ninth day.

COMMENT

The cause of death in acute morphine poisoning is asphyxia secondary to central respiratory depression, and the primary concern in treatment is the maintenance of oxygenation. Circulatory collapse occurs late and is secondary to anoxia. The importance of oxygen therapy and vigorous use of respiratory stimulants cannot be overemphasized. It has been said that 10% carbon dioxide inhalation may aid in respiratory stimulation in these patients.¹ Secondary considerations in treatment are measures to prevent aspiration and pneumonitis, maintenance of fluid and electrolyte balance, and catheterization for bladder distention. Nausea, pruritus, and obstipation call for symptomatic relief. If the drug has been taken by mouth, gastric lavage may be helpful, since spasm of the pyloric sphincter produces gastric retention and a considerable portion of the ingested drug may remain in the stomach for several hours.

The toxic dose of morphine in human beings varies widely. It is well known that comparatively small doses may result in severe depression in infants, the aged, and patients with chronic lung disease, severe liver damage, myxedema, or adrenal cortical insufficiency. Whereas marked tolerance for the drug is developed in addicts, a dose of 60 mg. is usually toxic for normal adults, and

From the Medical Service, Grady Memorial Hospital, and the Department of Medicine, Emory University School of Medicine.
1. Tovell, R. M.: Treatment of Acute Morphine Poisoning, Proc. Staff Meet. Mayo Clin. 8: 646-648, 1933.

250 mg. is usually fatal.² Survival after much larger amounts has been reported, however, as summarized in the accompanying table.

The occurrence of abdominal pain and tenderness in this patient, together with the striking elevation in serum amylase activity, suggests strongly that pancreatitis developed. This is of great interest in view of recent reports emphasizing the elevation of serum amylase after opiates, presumably due to spasm of Oddi's sphincter.³

SUMMARY

A case with recovery after intravenous injection of 0.76 gm. of morphine sulfate is reported. The therapy of acute morphine poisoning is discussed briefly, and reported recoveries following large doses of this drug are tabulated. An interesting feature of the present case was the development of severe epigastric pain and tenderness concomitant with significant elevation in serum amylase activity, suggesting pancreatitis.

2. Goodman, L., and Gilman, A.: *The Pharmacological Basis of Therapeutics: A Textbook of Pharmacology, Toxicology and Therapeutics for Physicians and Medical Students*, New York, The Macmillan Company, 1941, p. 209.

3. Myhre, J.; Nesbitt, S., and Hurly, J. T.: Response of Serum Amylase and Lipase to Pancreatic Stimulation as a Test of Pancreatic Function: Mecholy Secretin and Morphine Secretin Tests, *Gastroenterology* 13: 127, 1949. Burke, J. O.; Plummer, K., and Bradford, S.: Serum Amylase Response to Morphine, Mecholy and Secretin as a Test of Pancreatic Function, *Gastroenterology* 15: 699-707, 1950. Gross, J. B.; Comfort, M. W.; Mathieson, D. R., and Power, M. H.: Elevated Values for Serum Amylase and Lipase Following the Administration of Opiates: A Preliminary Report, *Proc. Staff Meet., Mayo Clin.* 26: 81-87, 1951.

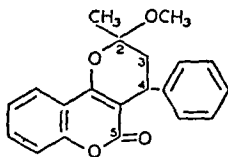
COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, M.D., Secretary.

Cyclocumarol.—Cumopyran (Abbott).—3,4-Dihydro-2-methoxy-2-methyl-4-phenyl-2H,5H-pyrano[3,2-c][1]-benzopyran-5-one. $C_{20}H_{18}O_3$.—M.W. 322.34.—The structural formula for cyclocumarol may be represented as follows:



Actions and Uses.—Cyclocumarol, a synthetic anticoagulant related chemically and therapeutically to bishydroxycoumarin, produces its effect by lowering the blood concentration of prothrombin. It is useful, therefore, in the prophylaxis and treatment of intravascular clotting for the same purposes which have been recognized for other similar anticoagulants. See the monograph on Bishydroxycoumarin.

Cyclocumarol is approximately two to three times as potent as bishydroxycoumarin and its onset of effect is sometimes more rapid and often somewhat more prolonged. However, studies so far completed do not substantiate the view that cyclocumarol may be less toxic to small blood vessels and capillaries than

therapeutically equivalent amounts of other anticoagulants or that its use minimizes frequent variations in the prothrombin level, which may occur with shorter-acting anticoagulants.

Cyclocumarol is effective orally and should be administered with the same precautions observed for similar anticoagulants to avoid overdosage and hemorrhage. Little or no gastrointestinal disturbance has been encountered with its use. Facilities should be available for making daily prothrombin determinations to prevent overdosage, for blood transfusion, and for parenteral administration of vitamin K for the treatment of overdosage. Patients should be regularly observed for evidence of bleeding.

Dosage.—Initially, 0.1 to 0.2 gm. is administered orally depending on the size and condition of the patient and the prior blood prothrombin level. Somewhat smaller doses are usually sufficient for patients with cardiac decompensation or myocardial infarction. The onset of effect usually occurs within 24 hours and the full therapeutic effect on prothrombin activity is usually reached within 36 hours. After the initial dose, prothrombin activity is determined daily for the first 10 days to estimate the daily dosage to be administered at one time. If prothrombin activity exceeds 25%, a 12.5 to 50 mg. total daily dose is administered. Occasionally, it may be necessary to stop administration of the drug on days when the prothrombin activity is 25% or less.

Tests and Standards.—

Physical Properties: Cyclocumarol is a white, crystalline powder with a slight odor. It melts between 164 and 168°. It is insoluble in water and slightly soluble in alcohol.

Identity Tests: A 0.015% solution of cyclocumarol, prepared as directed later in the assay, exhibits ultraviolet absorption maxima at 2,710 and 2,820 Å, and a minimum at 2,760 Å. The ratio of the specific absorbancies at 2,760 and 2,710 Å. is not less than 0.897 nor more than 0.997, and the ratio of the specific absorbancies at 2,760 and 2,820 Å. is not less than 0.856 nor more than 0.956.

Purity Tests: Test for heavy metals as directed in U. S. P. XIV, page 717: the turbidity developed does not exceed that of a control containing 30 ppm of lead.

Dry about 1 gm. of cyclocumarol, accurately weighed, at 105° for 2 hours: the loss in weight is not more than 1.0%.

Ash about 2 gm. of cyclocumarol, accurately weighed: the amount of ash is not more than 0.2%.

Assay: (Cyclocumarol) Transfer about 0.1 gm. of cyclocumarol, accurately weighed, to a 100 ml. volumetric flask, dissolve in alcohol with the aid of gentle heat, cool, fill to the mark with alcohol and mix well. Transfer exactly 10 ml. of this solution to a second 100 ml. volumetric flask and fill to the mark with alcohol. Transfer exactly 15 ml. of this solution to a third 100 ml. volumetric flask and dilute to the mark with alcohol to give a final concentration of about 0.15 mg. per milliliter. Determine the absorbancy of this solution at 2,820 Å. with a spectrophotometer. The number of milligrams present per milliliter of the final solution = absorbancy at 2,820 Å. ÷ 396. The amount of cyclocumarol present is not less than 97.0 nor more than 103.0%.

Dosage Forms of Cyclocumarol

Tablets. **Assay:** (Cyclocumarol) Weigh 20 tablets and grind them. Transfer to a 100 ml. volumetric flask an amount of powder, accurately weighed, equivalent to about 0.1 gm. of cyclocumarol. Fill to the mark with alcohol and mix thoroughly. Proceed as directed in the assay in the monograph for Cyclocumarol starting with, "Transfer exactly 10 ml. of this solution . . ." The amount of cyclocumarol present is not less than 95.0 nor more than 105.0% of the labeled amount.

Tablets Cumopyran: 25 mg. and 50 mg. Manufactured by license from Wisconsin Alumni Research Foundation under U. S. Patent 2,427,529. Abbott Laboratories, North Chicago, Ill.

Sodium p-Aminosalicylate (See New and Nonofficial Remedies 1951, page 90).

Powder Parasal Sodium: 113.4 gm., 226.8 gm., and 453.6 gm. bottles. Bulk: 11.34 kg. and 22.68 kg. drums for compounding use. U. S. Trademark 585,718. The Panray Corporation, New York.

Tablets Parasal Sodium: 0.5 gm. U. S. Trademark 585,718. The Panray Corporation, New York.

Capsules Pasara Sodium: 0.5 gm. Smith-Dorsey Company, Lincoln, Neb.

Powder Pasara Sodium: 454 gm. bottles, and 11.34 kg. containers. Smith-Dorsey Company, Lincoln, Neb.

Pyridoxine Hydrochloride (See New and Nonofficial Remedies 1951, page 445).

Tablets Pyridoxine Hydrochloride: 5 mg. and 25 mg. Physicians' Drug & Supply Company, Philadelphia.

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FROSTBITE

While frostbite occurs only sporadically in civilian populations, it is a major cause of disability among military personnel in temperate and arctic climates or at high altitudes. During World War II it incapacitated several hundred thousand men in various armies, and in the Korean conflict it has produced over 5,000 United Nations casualties. As a consequence, research on the problem has been accelerated, and a variety of methods of treatment, both new and old, have been subjected to controlled testing. While the results have not always been conclusive, they have forced a reversal of opinion on at least one time-honored principle of treatment and have indicated that several additional therapeutic measures may have some value.

Opinion has been reversed with respect to the relative merits of slow and rapid thawing of the frozen part. Until recently, custom sanctioned slow thawing, presumably because this produces less pain than rapid thawing. Controlled observations, however, have shown that slow thawing with ice water, ice bags, cold packs, or cold air increases the extent of necrosis following frostbite,¹ while rapid thawing at a temperature of 40 to 42 C reduces the damage.² Emphasis is placed on the fact that the temperature at which the part is rewarmed must be carefully controlled. Thawing at 38 C is not so effective in reducing tissue damage as thawing at 42 C.³ On the other

hand, rewarming at temperatures above 50 C seems to be harmful rather than beneficial. It appears further that external heat should be removed from the affected part as soon as thawing is complete. In one experiment^{1a} frozen mouse tails kept in air heated to 40 C for 72 hours after rapid thawing showed more gangrene than those left at room temperature (20 C) after thawing. On the basis of German experience during World War II, Killian⁴ suggested that heating of the trunk should precede thawing of the frozen distal part. This procedure, which produces vasodilatation in the extremities, is employed to increase the supply of oxygen to the frozen tissues before their metabolic demands are increased by local heat. Under field conditions where the entire body as well as the frozen part is exposed to cold, early and active warming of the trunk would seem to be a logical measure, but local thawing should probably be carried out simultaneously, since delay in local thawing has been shown to increase tissue damage.

Additional therapeutic measures evaluated have included those designed to eliminate the vasospasm, sludging of blood, and thrombosis that occur during certain stages of the freezing process. These reactions are believed by many investigators to be the primary cause of tissue necrosis, but Lewis⁵ has questioned this view. In recent experiments he has shown that extensive necrosis can occur during freezing independently of vascular thrombosis or spasm. It cannot be denied, however, that vascular stasis and thrombosis do occur in frozen tissue, and, while they may not be the primary cause of necrosis, it seems likely that they contribute to it and to delayed healing. The experimental evidence on the therapeutic effect of vasodilating procedures has been reviewed by Shumacker and Lempke.^{1b} These authors conclude that interruption of the sympathetic nerve supply to the frozen area by procaine block or sympathectomy may be beneficial in the early treatment of frostbite but that systemically administered autonomic blocking agents are unreliable in bringing about vasodilatation of the extremities, particularly in the presence of pronounced vasospasm. The use of heparin to reduce agglutination of sludged erythrocytes and minimize thrombosis has been found by some investigators to diminish the incidence of gangrene following frostbite in animals⁶ and to have a beneficial effect in man.⁷ Other workers⁸ have found it to be of no value, but according to Lange⁹ this is due to their failure to depress prothrombin levels continuously for several days. Further trials of anticoagulants in man seem justified.

Tests have also been carried out with measures designed to reduce the increased vascular permeability and edema that occur during thawing of frozen tissues. Antihistaminic drugs have been employed on the assumption that this vascular reaction is due to the liberation of a histamine-like substance from damaged cells. The evidence suggests that these drugs may be of some benefit.¹⁰ Rutin also has been reported¹¹ to diminish tissue damage in some species following frostbite, but there is little information on the clinical usefulness of either of these drugs in man. Cortisone¹² and corticotropin¹³ have not reduced

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2. Adams-Ray, J., and Falconer, B.: Pathologico-Anatomical Changes Following Rapid and Slow Thawing, Respectively, in Frozen Skin in Man, *Acta chir. scandinav.* **101**:269, 1951. Fuhrman, F. A., and Crismon, J. M.: Studies on Gangrene Following Cold Injury: Treatment of Cold Injury by Means of Immediate Rapid Warming, *J. Clin. Investigation* **26**:476, 1947. Lewis, R. B.: Microwave Diathermy Treatment of Frostbite, *Proc. Soc. Exper. Biol. & Med.* **78**:163, 1951. Shumacker and Lempke.^{1b}

3. Finneran, J. C., and Shumacker, H. B., Jr.: Studies in Experimental Frostbite: Further Evaluation of Early Treatment, *Surg., Gynec. & Obst.* **90**:430, 1950.

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5. Lewis, R. B.: Local Cold Injury—Frostbite, *Mil. Surgeon* **110**:25, 1952.

6. Lange, K., and Boyd, L. J.: Functional Pathology of Experimental Frostbite and Prevention of Subsequent Gangrene, *Surg., Gynec. & Obst.* **80**:346, 1945. Lempke and Shumacker.^{1a}

tissue necrosis in animals. Pressure dressings to reduce edema have had no beneficial effects in the experience of Shumacker and Lempke.^{1b}

Other measures used in severe frostbite, such as administration of antibiotics or chemotherapeutic agents to prevent secondary infection and the careful débridement of necrotic tissue, are accepted as routine by most workers. Early active and passive motion has been recommended to stimulate circulation, prevent contractures, and minimize muscular atrophy.

It is evident that much more clinical testing in man will be necessary before the value of many of these procedures can be firmly established. The large scale studies now being carried out by the armed forces in Korea are a forward step in this direction.

BRONCHOSCOPY IN THE NEWBORN

It has been estimated that the total infant mortality in the United States in the first few days of life exceeds 120,000 per year and that about one-fifth of the deaths during the first two days of life are produced by asphyxia and related conditions.¹ Immaturity contributes to the largest number of neonatal deaths, followed by birth injury, congenital malformations, postnatal asphyxia and atelectasis. Moreover, asphyxia, even though it does not necessarily prove fatal, can produce alterations in cerebral tissue that will not be immediately evident but that will become apparent in later life. The various pathological entities responsible for alterations in respiration in most instances are probably irreversible, yet there are contingencies in which accurate diagnosis and appropriate treatment save life.

Among the devices that have been proposed to resuscitate the newborn infant are the administration of oxygen mixed with small amounts of carbon dioxide, cleansing of the upper respiratory passages and the trachea by catheter suction, artificial respiration, drug stimulation, suspension of the infant with head down, mouth to mouth breathing, and stimulation by immersion alternately in warm and cold water. The lives of numerous newborn infants no doubt have been saved by the prompt application of some of these procedures.² Many bronchoscopists believe that additional lives could be saved and subsequent respiratory complications of the neonatal period be reduced by the wider use of the bronchoscope in selected cases at a time when newborn infants fail to respond promptly to well-established measures. The assistance that the endoscopist can give in handling problems of resuscitation and aspiration of the newborn is not as widely recognized nor as extensively utilized as it should be.

Despite the need for additional experience in establishing the indications and contraindications for bronchoscopy in the newborn, the bronchoscopic procedure is an important salvage measure. The cooperation of obstetricians, pediatricians, and endoscopists might conceivably reduce both the morbidity and the mortality rates of the newborn. The designation of a small room adjacent to delivery rooms in hospitals for the purpose

of meeting respiratory emergencies of the newborn would invite progress in the field.³ Finally, in order to establish his value as consultant, the bronchoscopist should be available for emergencies⁴ at all hours.

DDT RESISTANT BODY LICE

Hurlbut¹ and associates of the Eighth U. S. Army in Korea report that contrary to their expectations routine application of 10% DDT powder to a large group of military personnel during the winter and spring of 1951 resulted only in a steady increase in their infestation with body lice. Since previous laboratory experiments had shown that DDT resistant strains of houseflies can be developed by selective breeding, the army officers compared the DDT resistance of local body lice with that of routine laboratory strains. They found that when groups of 20 local lice were confined within treated sleeves, which could be worn, thus permitting normal feeding, from 40 to 60% of them remained alive at the end of 48 hours exposure to DDT powder. Under similar conditions there was a 100% mortality among standard laboratory strains of body lice. Local lice were also reared throughout their entire life cycle on cloth impregnated with 0.1% DDT solution in acetone, cloth impregnated with 0.05% solution being lethal for standard laboratory lice.

From these and other data it was concluded that DDT resistant body lice were prevalent in certain Korean areas, presumably as a result of local selective breeding. From this it follows that the routine use of DDT powder for the control of typhus might be ineffective in certain localities.

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8. (a) Quintanilla, R.; Krusen, F. H., and Essex, H. E.: Studies on Frostbite with Special Reference to Treatment and Effect on Minute Blood Vessels, *Am. J. Physiol.* **149**: 149, 1947. (b) Fuhrman, F. A., and Crismon, J. M.: Studies on Gangrene Following Cold Injury: Effect of Rutin and Other Chemical Agents on Course of Experimental Frostbite in Rabbits, *J. Clin. Investigation* **27**: 364, 1948. (c) Pichotka, J., and Lewis, R. B.: Use of Heparin in Treatment of Experimental Frostbite, *Proc. Soc. Exper. Biol. & Med.* **72**: 130, 1949.

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11. Fuhrman and Crismon,^{8b} Shumacker, Radigan, Ziperman and Hughes.^{10b}

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13. Lempke, R. E., and Shumacker, H. B., Jr.: Studies in Experimental Frostbite: Treatment with ACTH, *Angiology* **2**: 340, 1951.

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3. Jackson, C. C. R.: Bronchoscopy in the Newborn, *Ohio M. J.* **46**: 869 (Sept.) 1950.

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ORGANIZATION SECTION

STATEMENT OF A. M. A. REPRESENTATIVE ON PROPOSED NEW DEPARTMENT OF HEALTH BEFORE SENATE COMMITTEE

Mr. Chairman and members of the Committee: My name is Walter B. Martin. I am engaged in the active practice of medicine in Norfolk, Va., and am also a member of the Board of Trustees of the American Medical Association. I am appearing here today on behalf of that Association in opposition to S. 1140, 82d Congress. This bill, which is intended primarily to effect the medical recommendations of the Hoover Commission on Organization of the Executive Branch of the Government, would provide for the transfer of various federal medical services to a new Department of Health. The major health services included would be the Department of Medicine and Surgery of the Veterans Administration, most of the hospitals and other medical facilities of the armed services, and the United States Public Health Service. A secretary of cabinet rank would head the proposed new department and would be assisted by an advisory board composed of the Secretary of Defense, the Administrator of Veterans' Affairs, and the Surgeon General of the Public Health Service.

Before discussing the specific provisions of the pending bill and the position of the American Medical Association with respect thereto, I would like to review briefly the pertinent recommendations of the Hoover Commission on Federal Medical Activities. The Hoover Commission's report in this regard was presented in March, 1949, based on reports received from its Medical Task Force in January and February of 1949. Although the report did recommend, in part, the program proposed by S. 1140, the basic or primary recommendations of the commission were (a) that the Congress clearly define the beneficiaries entitled to medical care from the federal government and the relative priorities of such beneficiaries and (b) that the present inconsistencies in the federal hospital construction program be resolved. The Task Force, in conducting the studies prior to the issuance of its report, found that the existing federal medical program was "devoid of any central plan" and concluded that there must be over-all planning, which would require "first a clear definition of the extent of the responsibilities, and second an organization appropriate to carry out the commitment."

It would seem, therefore, that, although S. 1140 would establish the agency for carrying out the commitment, the primary recommendations, which are in actuality conditions precedent to the consolidation of hospital facilities, have been ignored. It should also be noted that, despite the validity of certain of the recommendations of the Hoover Commission at the time of the issuance of the report in 1949, such proposals are not necessarily applicable today, owing in part to the hostilities in Korea and to the threat of war in various other parts of the world. Despite the fact that the American Medical Association is in favor of the establishment of a Department of Health and is in wholehearted accord with the desire to effect economy in the operation of federal medical services, it is the belief of the Association that S. 1140 will not accomplish the desired results.

The American Medical Association has repeatedly pointed out the wastefulness of the present uncoordinated system for providing medical care and hospital benefits by the federal government. Testimony to this effect was presented before the Senate Committee on Labor and Public Welfare during the 81st Congress on a similar bill, S. 2008. Since that time the Board of Trustees of the Association has on several occasions (most recently on Feb. 8, 1952) reiterated its belief that the real way to institute governmental economy in the use of funds and medical manpower is (a) to obtain a clear congressional definition

of the extent of the government's responsibility for furnishing medical care with particular reference to the treatment of veterans with non-service-connected disabilities and the dependents of service personnel and (b) to establish a federal board to control the distribution of beds among the several federal hospital services, to insure joint planning in the field of hospital construction, and to determine the need and location of proposed new hospitals in the United States.

In addition to the very vital objections referred to above, there are several specific provisions of S. 1140 with which the Association is not in agreement. In view, however, of the basic nature of the Association's opposition to the bill, any discussion of these items, with one exception, will be omitted. The most important of these specific provisions and the one on which I should like to comment briefly deals with the suggested inclusion of the medical facilities of the armed services and the Veterans Administration in the new Department of Health. It is the belief of the Association that such a transfer would be difficult at this time without sacrificing the quality of the service rendered and without seriously hampering the primary mission of the armed services and the Veterans Administration. Such a transfer of military installations, although questionable enough even in peacetime, would be fraught with danger during the present emergency.

This concludes my formal statement. I want to thank the committee for the privilege of presenting the views of the American Medical Association on this bill. I shall be happy to attempt to answer any questions that the members of the committee may have.

FEDERAL MEDICAL LEGISLATION

Social Security Amendment

Representative Cole of New York introduced H. R. 6719, which would amend title 2 of the Social Security Act to provide that persons may elect not to receive old age and survivors' insurance coverage with respect to self-employment.

Industrial Safety

Senator Murray of Montana introduced S. 2714, which would provide for assistance to state agencies administering labor laws in their efforts to promote, establish, and maintain safe work places and practices in industry, thereby reducing human suffering and financial loss, and increasing production through safeguarding available manpower. The bill provides that an unspecified amount of money would be provided by the federal government, so that the Secretary of the Department of Labor could allocate funds based upon a formula to the several states for industrial safety programs. States to be eligible would be required to meet standards set forth in the bill. The formula would be based on population, number of wage earners, special industrial hazards, number of workers afforded protection, the cost of state administration, and the financial means of the states. No state could receive more than three-fourths of its total expenditures from the federal government. A minimum allotment for each state would be \$15,000.

Regulation of Fireworks

H. R. 6722 was introduced by Representative McGuire of Connecticut and would designate the Bureau of Mines of the Department of Interior as the official agency for regulation of

The summary of federal legislation was prepared by the Washington Office of the American Medical Association and the summary of state legislation by the Bureau of Legal Medicine and Legislation.

fireworks in interstate commerce. The Bureau of Mines would be authorized to make regulations covering the sale and shipment of fireworks and would be the licensing agency for persons and firms engaged in manufacturing, processing, or importing fireworks. Persons or firms offering to sell, selling, offering to ship, or shipping any fireworks in violation of the regulations would be subject to both fine and imprisonment.

Transfer of Hospitals Between the VA and Department of Defense

Representative Rankin of Mississippi introduced H. R. 6724 at the request of the Department of Defense. It would permit the transfer of hospitals and other facilities, without reimbursement, between the Veterans Administration and the Army, Navy, and Air Force. Veterans Administration officials stated that under existing law, the VA can acquire hospital facilities from the Department of Defense without transfer of funds; however, the Defense Department may not acquire hospitals from the VA without transfer of funds.

Universal Military Training

Representative Brownson of Indiana introduced H. R. 6765, which proposes the establishment of a National Security Training Corps and provides for its administration and discipline. The plan contained in this bill was first submitted during the House public hearings on universal military training by the author and Representatives Lantaff of Florida and Curtis of Missouri. They suggested a ROTC program for all males in their last two years of high school. The program would cover a period of five hours per week, lasting two years, for a total of 320 hours of training.

School Health Safety and Physical Education

Representative Elliott of Alabama introduced H. R. 6720, which would authorize the appropriation of funds to assist the states and territories in extending and improving their program of health instruction, safety instruction, and physical education, for children of school age. This bill is identical with H. R. 5853, previously reported.

STATE MEDICAL LEGISLATION

Arizona

Bills Introduced.—H. 231 and S. 83 propose the creation of an Arizona commission on alcoholism to establish a program for the rehabilitation of alcoholics and to provide for the medical, psychiatric, and other scientific treatments for chronic alcoholics and for other purposes.

Kentucky

Bills Introduced.—H. 323, relating to tuberculosis, proposes, among other things, that every practicing physician, or executive officer of tuberculosis institutions, shall notify the health officer of the county in which the persons afflicted reside of every case of tuberculosis which comes to his professional knowledge. H. 357, proposes to direct the commissioner of the state police to establish, equip and maintain a criminal identification section for the purpose of receiving and filing fingerprints, photographs, and other records pertaining to the investigation of crime and the apprehension of criminals. H. 385, proposes regulations for the licensing of persons desiring to practice ophthalmic dispensing. S. 238, to amend the workmen's compensation act, proposes that employees and employers shall furnish to the opposite party copies of any medical examinations made of the employee either by a physician chosen by the employer or by the employee's own physician.

New Jersey

Bills Introduced.—A. 419, to amend the temporary disability benefits law, proposes, among other things, to require payment for illness or disability due to pregnancy or resulting childbirth or miscarriage. A. 427, proposes to increase the penalty for a violation of any provision of the health ordinance from \$100 to \$200. A. 433, proposes the creation of a medical college to be known as the New Jersey State College of Medicine. S. 147, proposes regulations for the licensing of persons desiring to practice ophthalmic dispensing.

New York

Bills Introduced.—A. 2332 and S. 2227 to amend the labor law, propose the creation of an industrial council to advise the labor commissioner with respect to matters submitted to it. A. 2351, to amend the education law, proposes an appropriation for the purpose of creating subsidies for student nurses. A. 2426, to amend the correction law, proposes to authorize the commissioner of correction, when an emergency exists by reason of a lack of a sufficient number of physicians, to present evidence thereof to the civil service commission, which may determine the existence of an emergency and may waive the requirements of the civil service law as to the citizenship of applicants in competitive examinations for physicians in institutions under the control of the commission of correction. A. 2523, to amend the education law relating to optometrists, proposes to provide that the license of an optometrist shall not be revoked by reason of the act or conduct of any employer of such optometrist. A. 2527, proposes an appropriation to the state department of health for the purpose of conducting experiments in cooperation with the medical society of New York State in mass detecting diseases in their early stages through the process of multiphasic screening. A. 2539, to amend the education law, proposes to exempt from the labeling requirements proprietary medicines, except those proprietary medicines which are poisonous, habit forming and/or because of their toxicity or other potentiality for harmful effect, or of the method of their use, or the collateral measures necessary to their use, are not safe for use under the supervision of a practitioner licensed by law to administer such proprietary medicines. A. 2541, to amend the education law, proposes that courses of study beyond the elementary schools shall provide for instruction in the nature and effect on the human system of narcotics and habit-forming drugs. A. 2629, to amend the education law, proposes to authorize school districts to furnish special services, including physiotherapy, occupational therapy, and so forth, to children with cerebral palsy. A. 2737, to amend the disability benefits law, proposes that benefits under such law shall include the cost of providing disabled persons with the same medical, surgical or other attendance and treatment, nurse and hospital service as is provided under the workmen's compensation law. A. 2790, to amend the penal law, proposes that no person or organization operating a hospital, sanitarium or other institution shall permit the use of an ambulance to transport the persons to the hospital unless there is in attendance upon such ambulance at all times a duly qualified physician or intern who is a member of or connected with the staff of the institution. A. 3022, to amend the education law, proposes to define physician as including practitioners of osteopathy and naturopathy and provides for the licensing of naturopaths. A. 3046, to amend the workmen's compensation law, proposes to authorize injured employees to select to treat them any podiatrist authorized by the chairman of the industrial board to render podiatry care. S. 2311, proposes to authorize the fluoridation of the public water supplies in particular areas after consultation with the commissioner of health and recognized medical and dental authorities. S. 2483, proposes an appropriation to the education department for additional state scholarships for professional education in medicine and dentistry. S. 2544, to amend the public health law, proposes the establishment of a division of narcotic control in the department of public health. S. 2553, to amend the public health law, proposes to require every physician to give notice to the health officer of the county, city, town or village where such person resides, of every case of addiction which comes under his care.

Virginia

Bills Introduced.—H. 132, to amend the uniform narcotic act, provides, among other things, that the term "opiate" shall include all synthetic drugs having addiction forming or addiction sustaining properties similar to morphine and so proclaimed by the President of the United States under the provisions of the federal narcotic law. It also proposes special penalties where the offense charges consists of the sale of marijuana or narcotics to a minor. H. 426, proposes to make it unlawful for any employer to require an employee or applicant for employment to pay the cost of a medical examination or the cost of furnishing any records required by the employer as a condition of employment. S. J. R. 27, proposes to direct the Virginia advisory legislative council to make a study and to report upon the feasibility of establishing a pool for prepayment of hospital costs and other types of medical care for public assistance recipients. S. J. R. 42, proposes to direct the Virginia advisory legislative council to make a thorough study of ophthalmic dispensing and dispensing opticians and of statutes designed for the protection of the public interest in reference to such persons. S. 326, proposes to require the commissioner of mental hygiene and hospitals, upon the request of any judge, to furnish a list of psychiatrists from public or private mental clinics or hospitals having on their staffs psychiatrists qualified to make examinations of persons charged with certain crimes. The proposal would permit the accused to have the right to be examined by a psychiatrist of his own choice in addition to the examination performed by psychiatrists appointed by the court.

MEDICAL NEWS

ARKANSAS

Dr. Dodd to Head Pediatric Department.—Dr. Katherine Dodd, associate professor of pediatrics at the University of Cincinnati College of Medicine, has been appointed professor of pediatrics and head of the department at the University of Arkansas School of Medicine, Little Rock.

CALIFORNIA

Society News.—At a recent meeting of the Los Angeles Society of Allergy, Dr. Norman M. Shure, Los Angeles, was elected president and Dr. Ben C. Eisenberg, Beverly Hills, secretary-treasurer.

Radioactive Cobalt Chamber at U. C. L. A.—Installation of a new radioactive cobalt (Co^{60}) chamber in the Atomic Energy Project on the Los Angeles campus of the University of California was announced Feb. 18. Weighing more than eight tons, the chamber is constructed mainly of $8\frac{1}{2}$ in. lead. The Co^{60} source has an intensity of 100 curies, with a radiation output equivalent to about 100 gm. of radium. Made at the atomic pile at Oak Ridge National Laboratories, the U. C. L. A. sample of cobalt metal weighs only about 30 gm. The chamber will be used mostly for basic scientific studies of the effects of radiation. The chamber is one of three in the United States.

Donations to Blood Bank.—A check for \$5,000 has been presented to the Irwin Memorial Blood Bank of the San Francisco Medical Society by Mrs. Clara L. Watson of Guerneville in memory of her brother, the late Dr. Charles Francis Griffin, who practiced his entire professional life in San Francisco. The money will be used to continue studies on blood preservation. These studies are being carried out in cooperation with San Francisco's two medical schools, the University of California Medical School, and the Stanford University School of Medicine. In November of last year Mrs. Watson presented an identical gift to the Sonoma County Community Blood Bank in Santa Rosa.

LOUISIANA

Physician Selected as Outstanding Citizen.—Dr. Henry E. Gautreaux, who has practiced in Covington for 46 years, was elected its outstanding citizen for 1951. Since 1948 he has served as coroner of St. Tammany Parish and is a member of the board of directors of the new mental hospital being built near Mandeville. Since 1914 he has been in Red Cross work and has served as president of the parish medical society, as delegate to the state medical society, and as a member of various committees.

MAINE

Health Council Studies.—Three studies have been undertaken by the Maine Health Council, according to the Maine Tuberculosis Association. These are (1) a study and analysis of the Health Code of Maine in order that indicated changes may be recommended to the next legislature; (2) a study to determine the relationships of local health councils to the state council, how the latter may help the local health groups attain greater effectiveness, and the relationships between the local councils and the individual members of the state council; and (3) a study of the possibilities of the council's conducting, through its member agencies, informational workshops on matters of public health, public health law, and general health resources for health officers of individual townships.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

MICHIGAN

State Society Commends Hillsdale County Cancer Detection.—The Hillsdale County Medical Society was honored with a certificate of commendation by the Michigan State Medical Society at the Michigan Clinical Institute, March 13, for "its pioneering effort in developing the Hillsdale Plan for Tumor Detection, the most practical plan yet devised for finding cancer in early and curable stages." In the four years of operation of the plan, 4,733 cancer detection examinations have been made. One hundred and six cancers have been found among the 2,365 persons examined, an incidence of 2.24%. Over 62% of these cancers were in early or only moderately advanced stages.

MINNESOTA

Annual Jackson Lecture.—The annual Clarence M. Jackson Lecture, sponsored by the Phi Beta Pi Fraternity, will be given on April 21 by Dr. John M. Adams, professor, department of pediatrics at the University of California at Los Angeles School of Medicine, at the University of Minnesota Medical School, Minneapolis. Dr. Adams will speak on the subject of "Respiratory Diseases—Changing Concepts," and will also take part in a continuation course on pediatrics for specialists at the Center for Continuation Study April 21-23.

NEBRASKA

Dr. Lee to Head Department.—Dr. Leroy W. Lee, since 1947 assistant professor of urologic surgery at the University of Nebraska College of Medicine, Omaha, has been appointed chairman of the department of urology. He succeeds Dr. Edwin Davis Sr., who will continue as professor of urology at the college.

Honored for Long Service.—Three Omaha physicians on the faculty of Creighton University School of Medicine received plaques in recognition of 25 years of service at a Founders Day dinner in December. Those honored were Drs. Arthur C. Johnson, associate professor of surgery; James G. Vetter, instructor in surgery, and M. William Barry, associate professor of medicine.

Demonstration of Advantages of Rural Practice.—The Rural Medical Service Committee of the Nebraska State Medical Association is sponsoring a program March 27 with a long-range objective of encouraging Nebraska trained doctors to return to their home state for medical practice. The program will honor the senior medical students at both Creighton University School of Medicine, and the University of Nebraska College of Medicine in Omaha, and will demonstrate the advantages of medical practice in Nebraska.

NEW JERSEY

Society News.—At the December meeting of the New Jersey Neuropsychiatric Association Dr. David J. Flicker, Newark, was elected president; Dr. C. Archie Crandell, Greystone Park, president-elect; Dr. J. Lawrence Evans Jr., Englewood, secretary, and Dr. Frank P. Pignataro, Red Bank, treasurer.

Hospital Affiliates with Medical Center.—Overlook Hospital, Summit, has become affiliated with the New York University-Bellevue Medical Center in New York City under the center's regional hospital plan. The arrangement is designed to bring to practicing physicians in suburban and rural nonteaching hospitals the advantages of a working relationship with a university medical center. The plan is now serving hospitals in Connecticut, New Jersey, New York, and Pennsylvania. Overlook Hospital is a voluntary hospital having 145 beds and 41 bassinets and about 5,000 admissions a year. A new building program is underway, in which two six story wings, accommodating 206 beds, are to be completed during the next two years. The hospital serves an estimated 150,000 persons in the Summit area.

NEW YORK

Public Health Appointments.—Dr. Robert M. Albrecht has received permanent appointment to the position of associate public health physician (Communicable Disease Control), Bureau of Epidemiology and Communicable Disease Control of the state department of health, effective Jan. 1. Effective Jan. 15, Dr. Evan W. Thomas, New York, was given provisional appointment to the position of associate public health physician (Venereal Disease Control), Bureau of Venereal Disease Control. Dr. Ruth K. Beecroft has been appointed consultant pediatrician to the New York State Department of Health's Bureau of Maternal and Child Health. Dr. Beecroft has been with the Bureau of Maternal and Child Welfare of the Washington, D. C., Health Department.

New York City

Medical School Alumni Day.—The annual Alumni Day of the Long Island College of Medicine and the State University of New York at New York City College of Medicine will be held on April 26. A scientific session at Polhemus Clinical Hall will be followed by the annual business meeting. There will be interfraternity activity in the afternoon, followed by the 72nd annual dinner at the Columbus Club, One Prospect Park West, Brooklyn, at 7 p. m.

Society News.—The Section on Allergy of the Medical Society of the County of Kings and the Academy of Medicine of Brooklyn on March 11 heard Dr. William B. Sherman of Columbia University College of Physicians and Surgeons, speak on "Clinical Aspects and Management of Drug Allergy."—Mr. Leonard Katz will present a paper, "High Speed Processing of Film Using Turbulent Fluids," at the monthly conference of the New York Institute of Clinical Oral Pathology March 31 at the New York Academy of Medicine at 9 p. m.

Dr. Falk to Lecture in Israel.—Dr. Henry C. Falk, director of gynecology and obstetrics, Beth Israel Hospital, and clinical professor of gynecology, New York University, left for Israel Feb. 15 for a six week tour of government and private hospitals in Israel. Dr. Falk was invited by the medical advisory board of the Hebrew University-Hadassah Medical School to demonstrate certain types of gynecological surgery. He has also been invited by Dr. Bernard Zondek, head of the gynecological department of the school, to lecture to the Jerusalem Medical Society on pelvic inflammatory diseases.

Personals.—On Feb. 12 Dr. Jan Ehrenwald of the psychiatric division of Kings County Hospital, Brooklyn, addressed the staff at the Veterans Administration Hospital, Northport, Long Island, and discussed "Psychodynamics of Telepathy and Related Phenomena."—Dr. Joseph D. Teicher has accepted the position of director of the Child Guidance Clinic of Los Angeles.—Dr. Alexander Brunschwig was elected to honorary membership in the National Society of Surgeons of Cuba at the annual meeting on Jan. 26 in Pina del Rey, Cuba, where he delivered an address before the society.

Consultation Alcoholism Clinic.—This clinic, devoted to the treatment and rehabilitation of problem drinkers employed by New York business concerns, opened Feb. 4 at University Hospital. A check for \$25,000 for operating expenses for the first year has been presented to Dr. Anthony J. Lanza, chairman of the industrial medicine department of New York University-Post Graduate Medical School. Other commercial and manufacturing organizations have been invited to support the program. Dr. Arnold Z. Pfeffer of the university will be the physician-in-charge of the staff of medical and psychiatric specialists at the clinic. The clinic expects to operate on an outpatient basis. Severely ill persons will be hospitalized.

Tuberculosis Association Director Dies.—Charles A. Freck, for 13 years executive director of the Queensboro Tuberculosis and Health Association and active in the field of tuberculosis for nearly a quarter century, died Feb. 12 in Flushing (Queens) Hospital and Dispensary, aged 45. Mr. Freck had been director of health and education for the Tuberculosis and Health Society at St. Louis, was named director of field service for the Illinois Tuberculosis Association in 1933, and four years later became executive secretary of the Missouri Tuberculosis Association.

Mr. Freck was vice-chairman of the Civic Defense Recruiting Office and a member of the public health committees of the Medical Society of the County of Queens. For six years he was secretary-treasurer of the Public Health Association of New York City and also secretary-treasurer of the Council of Tuberculosis and Health Associations of Greater New York.

Bureau for Handicapped Children.—The creation of this bureau and the designation of Dr. Helen M. Wallace as director was announced Feb. 19 by the health department. Fundamental to the work of the bureau's reorganized program will be the development of more adequate case finding procedures, the stimulation of research to prevent crippling conditions, and a community plan that will enable families who need this service to find it among the many groups that help the handicapped.

Under the state aid program the city and state share the cost of hospital and convalescent care for some 1,400 children each year who have orthopedic and cardiac conditions and pays for care for youngsters who have some eye and orthodontic conditions. The 29 diagnostic clinics that handle children with orthopedic handicaps, heart conditions, hearing, and eye defects are being reorganized. They will be brought into a close working relation with medical schools and with hospitals that have treatment facilities staffed by experts in the various fields.

NORTH CAROLINA

Piedmont Proctologic Society.—The annual March meeting of this society will be held March 29 at the Hotel Charlotte in Charlotte. The speakers and their subjects will include:

Glenn G. Perry, High Point, Pruritus Ani.
Leonard J. Rabhan, Savannah, Ga., Diverticulosis and Diverticulitis.
G. Farrar Parker, Asheville, Anal Carcinoma.

OKLAHOMA

Enid Blood Bank.—The American Red Cross Blood Center, through which Enid hospitals may be assured an adequate supply of blood and plasma at all times, has been opened as a subsidiary of the Wichita Red Cross Regional Blood Center. Establishment of the center in Enid was the culmination of plans begun in 1949 when the Garfield County Medical Society voted to sponsor the movement. The delay was occasioned by the lack of enough "bloodmobiles" to cover the territory and the reluctance of the Wichita, Kan., center to cross state lines. Subsidiaries of the Wichita Regional Blood Center have also been established in Bartlesville, Blackwell, and Newkirk.

PENNSYLVANIA

State Hospital Centenary.—Harrisburg State Hospital is celebrating its centenary with a series of meetings of ancillary groups. The hospital was founded by Dorothea L. Dix, and has become the keystone around which the Commonwealth of Pennsylvania has built a hospital system of 17 institutions housing almost 40,000 patients.

Public Health Council.—A permanent home for the Pennsylvania Health Council, which was formed in Harrisburg Feb. 11, 1950, by representatives of 43 health agencies of the commonwealth, was to be established about March 1 in Harrisburg. Created to "study health needs of the Commonwealth, to help develop and promote constructive health programs, and to propose constructive and needed legislation and to work for its enactment into law," the Pennsylvania Health Council also aims to prevent and eliminate overlapping and duplication of community health efforts. Among the member organizations of the council are the Association of the Junior League of America and the state groups of the League of Women Voters, Federation of Business and Professional Women's Clubs, Home Economics Association, Welfare Conference, and the Pennsylvania State College. The American Legion, National Foundation for Infantile Paralysis, Pennsylvania Public Health Association, and various hospital service associations, nursing organizations, medical schools, and the Medical Society of the State of Pennsylvania are also associated with the council. Officers include Dr. Gibson C. Engel, Philadelphia, president; Dr. C. Howard Witmer, Lancaster, first vice-president; William G. Mather, Ph.D., State College, secretary, and Mr. Edward M. Green, Harrisburg, treasurer.

Philadelphia

Postgraduate Institute.—The annual postgraduate institute and convention of the Philadelphia County Medical Society will be held April 1-4 at the Bellevue-Stratford Hotel. Arrangements are being made to televise special clinical programs from Jefferson Medical College Hospital directly to the lecture hall at the hotel on Wednesday, Thursday, and Friday mornings. Among the subjects to be covered at this year's meeting are ear, nose, and throat problems; obstetrics and gynecology; pediatrics; surgical problems, and dermatology. There will be panel discussions on corticotropin (ACTH), cortisone and hydrocortisone, functional problems in general practice, and the stroke problem. The customary clinical pathological conference will be held Thursday evening, and there will be many technical exhibits. The director of the institute is Dr. Thomas M. Durant, 301 S. 21st. St., Philadelphia 3.

Pittsburgh

Anesthesia Memorabilia.—W. Harry Archer, D.D.S., professor of oral surgery and anesthesia of the school of dentistry of the University of Pittsburgh, has placed on permanent loan to the Wood Library and Museum a large collection of anesthesia memorabilia. The collection, which is at present incompletely catalogued, includes 22 machines of various periods of historical interest.

RHODE ISLAND

Health Record Booklets.—The Health Department of the City of Providence now gives each child born in the city a health record booklet in addition to its birth certificate. This 16 page booklet contains information relative to the child's birth and provides space for its medical history through the fourth year of life. It will have pages for the results of preschool and school examinations and for recording specific defects and remarks.

TENNESSEE

Student Award for Overcoming Difficulties.—While some colleges award prizes to students with the best scholastic records, the University of Tennessee College of Medicine, Memphis, has announced plans to honor the student of each graduating class "who has overcome the most difficulties in obtaining a degree." The prize will be awarded to a member of the graduating class each quarter, beginning in March. A committee of classmates, with the aid of Mr. F. J. Montgomery, director of student welfare, will select the recipient. The prize will be purchased with funds contributed to the university by Dr. Charles C. Verstandig, radiologist, of New Haven, Conn., who graduated from the college in 1939.

TEXAS

Personal.—Dr. James Walter Long, medical director for Gulf Oil at Port Arthur, became medical director of the entire Gulf Oil Corporation Jan. 1, with headquarters in Pittsburgh. Dr. Long had been with the Gulf refinery since 1930. He has been a member of the state board of health since July, 1951.

Lecture Commemorating Birth of Leonardo da Vinci.—Dr. Elmer Belt, Los Angeles, will give an address at the University of Texas Medical Branch, Galveston, March 27 in commemoration of the 500th anniversary of the birth of Leonardo da Vinci (1452-1519), who contributed much to the development of anatomy. Dr. Belt, who will also discuss problems of renal excretion, has assembled important reference libraries relating to Leonardo da Vinci.

WEST VIRGINIA

Woman's Auxiliaries.—Two new local auxiliaries to component medical societies have recently been organized in West Virginia. They are the Woman's Auxiliary to the Hancock County Medical Society, and the Woman's Auxiliary to the Wyoming County Medical Society. The growth of the auxiliary in West Virginia has been phenomenal during the past three years. There are now 21 local auxiliaries as compared with 14 in 1949. The total membership, including members at large, is 971. Nurse recruitment is one auxiliary project.

ALASKA

Anchorage Chest Clinic.—In a community-wide effort to help combat tuberculosis, residents of Anchorage have acquired a chest clinic. It was first started as a diagnostic clinic in 1949 at the Anchorage Health Center, under the direction of Dr. Wendell C. Matthews, tuberculosis consultant for the Alaska Department of Health. The city remodeled space in the center for expansion of the clinic in 1950, and the Tuberculosis Committee of the Anchorage Health and Welfare Council arranged for the purchase of \$1,800 worth of equipment. Two other civic organizations contributed. The Alaska Department of Health supplied the x-ray machine, the fluoroscope, and the equipment for doing pneumoperitoneum; it also provides the services of the physician who conducts the clinic. The new clinic was officially opened in May, 1951. Up to Oct. 1, some 1,200 roentgenograms had been taken, which included a mass survey of all the food handlers in the city of Anchorage. Posthospitalization treatment for tuberculous patients is another of the important services of the clinic.

GENERAL

Postpone International Congress.—The Third International Congress of Legal and Social Medicine, which was to be held in Berne, Switzerland, April 15-18, has been postponed. It is hoped that the congress may be organized at a later date.

Society Election.—Newly elected officers for the American Academy of Orthopaedic Surgeons include Dr. Francis M. McKeever, Los Angeles, president; Dr. Harold B. Boyd, Memphis, president-elect; Dr. John R. Norcross, Chicago, secretary, and Dr. H. Relton McCarroll, St. Louis, treasurer.

College of Surgeons Exhibit Space.—The American College of Surgeons has space available for scientific exhibits at its clinical congress to be held in New York, Sept. 22-26, with headquarters at the Waldorf-Astoria. Application for this space should be made immediately to Walter E. Batchelder, M.D., Chairman, Committee on Scientific Exhibits, American College of Surgeons, 40 E. Erie St., Chicago 11.

Health Foundation to Study Industrial Health Plans.—Sheldon G. Lowry, research assistant in the department of sociology and anthropology at Michigan State College, Lansing, has become associated with the Health Information Foundation, New York, on a special assignment related to a study of health plans in industry. The foundation's industrial health research program is designed to determine the relationship between health programs in industry and productivity, absenteeism, labor turn-over, and other industrial relations factors.

Tropical Research Foundation.—A new foundation has been established in Chicago to support research in all phases of life in the tropics, under the name of Tropical Research Foundation in Chicago. The first chairman of the board of trustees is Mr. P. P. Vlcek, and the secretary is Mr. M. V. Tulsky. In 1952 the foundation is sponsoring an expedition to the Caribbean and Central and South America, headed by Dr. Oscar Felsenfeld of the Hektoen Institute. The resources of the foundation are donations from American industry and from private persons.

Dr. Kolmer Receives Dentistry Award.—Dr. John A. Kolmer, Philadelphia, will receive Sigma Epsilon Delta's annual award for outstanding contribution to dentistry at its convention in Wernersville, Pa., May 23-25. He was chosen for his untiring efforts to bring close cooperation between physicians and dentists. Dr. Kolmer is professor of medicine in the Medical and Dental Schools of Temple University and director of the Institute of Public Health and Preventive Medicine, Philadelphia. He is an honorary member of the American Academy of Dental Medicine and author of many books and papers.

Proposed International Congress of Medical Librarians.—It is proposed to hold an International Congress on Medical Librarianship in London in July, 1953. Sir Cecil Wakeley, K.B.E., C.B., president of the Royal College of Surgeons of England, has consented to accept the honorary presidency of the congress. The program will include formal sessions for reading and discussion of papers, visits to medical libraries, and social functions. It is hoped also to have an exhibition of medical books and

periodicals and library equipment. All those interested in medical librarianship throughout the world are invited to participate. Requests for information may be addressed to the Honorary Secretary, First International Congress on Medical Librarianship, in care of The London School of Hygiene and Tropical Medicine, Keppel St., London W.C.1.

New Editor for Internal Medicine Journal.—Dr. Paul W. Clough, Baltimore, has retired as editor-in-chief of the *Quarterly Review of Internal Medicine and Dermatology*. He was succeeded by Dr. Emanuel B. Schoenbach, New York, professor of medicine at the University of New York Medical Center at Brooklyn, and director of medical services at Maimonides Hospital, Brooklyn. Dr. Schoenbach has been on the faculty of Johns Hopkins University School of Medicine. He is a member of the committee on cancer diagnosis and therapy of the National Research Council and a consultant to the National Cancer Institute. Dr. Clough has been associated with Johns Hopkins University since his graduation there in 1907.

Courses in Radioisotopes.—Three additional courses in techniques of using radioisotopes in research will be offered by the special training division of the Oak Ridge Institute of Nuclear Studies this summer. Dates for the courses are: June 9 to July 4, July 7 to Aug. 1, and Aug. 11 to Sept. 5. The courses are designed to acquaint mature research workers with the safe and efficient use of radioisotopes in research. Each course is open to 32 participants. Information may be obtained from Ralph T. Overman, Chairman, Special Training Division, Oak Ridge Institute of Nuclear Studies, Oak Ridge, Tenn.

Meeting on Internal Medicine.—The North Pacific Society of Internal Medicine will hold its spring meeting March 22 in the library auditorium of the University of Oregon Medical School, Portland. Those speaking by invitation are as follows:

Daniel H. Labby, Portland, Inter-relationships of Kidney and Liver Disease.

Herbert E. Griswold Jr., Portland, Primary Pulmonary Hypertension in Children.

John T. Van Bruggen, Ph.D., and Tyra T. Hutchens, Portland, Cholesterol Metabolism.

At the dinner meeting at 6 p. m. Dr. Adolph Weinzirl, professor and head of the department of public health and preventive medicine at the University of Oregon Medical School, will speak on communication.

Essay Contest in Plastic and Reconstructive Surgery.—The Foundation of the American Society of Plastic and Reconstructive Surgery offers awards in junior and senior classifications for original contributions in their field. The junior classification offers two scholarships for six months in leading plastic surgery services in the United States, England, and Italy. The contest is open to plastic surgeons who have practiced the specialty not longer than five years. The senior classification prize is a silver plaque awarded for the best essay presented at the society's annual meeting. The winning essays will appear on the program of the annual meeting in New York in November. All entries must be received by the award committee not later than Sept. 1. For information address The Award Committee, c/o Jacques W. Maliniac, M.D., 11 East 68th St., New York 21.

Outbreaks of Foot-and-Mouth Disease.—The United States Agriculture Department late in February began tracing every animal imported recently from Canada after an outbreak of foot-and-mouth disease in the dominion. The department closed the Canadian border to imports of all cloven hoof animals and to imports of fresh and frozen meat. Incomplete reports listed outbreaks on at least 22 ranches in Saskatchewan, a province adjoining Montana and North Dakota, which ordinarily raises over 100 million pounds of meat and more than 360,000 head of cattle, swine, and sheep. A serious outbreak of foot-and-mouth disease in Mexico was recently eradicated at a cost of 100 million dollars. Three outbreaks of the disease have been discovered in Mexico in the last two years and the latest last August. The last outbreak in this country was halted about 20 years ago. Europe is reported to be experiencing one of its worst outbreaks. The

importation of animals and fresh or frozen meat from Argentina has been banned for years because of foot-and-mouth disease there.

Dr. Esmond Long Resigns as Secretary and Editor.—Dr. Esmond R. Long, Philadelphia, executive secretary of the American Trudeau Society since 1947, has resigned in order to devote more time to the National Tuberculosis Association's expanding program of medical research. Dr. Floyd M. Feldmann, Washington, D. C., assistant to the managing director, NTA, has been appointed acting executive secretary. Dr. Long also submitted his resignation as editor-in-chief of the *American Review of Tuberculosis*, official publication of the American Trudeau Society, taking effect Dec. 31, 1951; and Dr. Walsh McDermott, formerly managing editor, has been named editor. Dr. Long has been designated consulting editor. In addition to his duties with NTA, Dr. Long is director of the Henry Phipps Institute of the University of Pennsylvania, Philadelphia.

Industrial Health Conference.—This conference to be held at the Netherland Plaza Hotel, Cincinnati, April 19-26, will include meetings of six industrial health groups: the Industrial Medical Association, the American Conference of Governmental Industrial Hygienists, the American Industrial Hygiene Association, the American Associations of Industrial Dentists and Industrial Nurses, and the U. S. Navy Fourth Annual Industrial Organization. The Industrial Medical Association will hold clinics on Monday and Tuesday at Cincinnati General Hospital. At the general sessions of the association papers will be read by Dr. Lawrence E. Hinkle Jr., New York, "Life Stress and Industrial Absenteeism," and Dr. S. Charles Franco, Brooklyn, "Limitations of the Portal Ballistocardiograph in the Detection of Heart Disease." There will be a panel discussion on "Medical Service in Industry," with Dr. Robert C. Page, New York, as chairman. There will be joint meetings of the various groups. The annual banquet will be held at 6:30 p. m. on Wednesday.

Borden Awards.—For outstanding research in several fields last year, nine Borden Awards of a gold medal and \$1,000 have been given by the Borden Company Foundation. Since the awards were established in 1936 presentations have been made to 99 scientists. The 1951 recipients in the medical and related fields and the associations through which the awards are given include:

Edwin B. Astwood, research professor of medicine, Tufts College Medical School, Boston, for research in endocrinology with special reference to hyperthyroidism, the Association of American Medical Colleges.

Daniel C. Darrow, professor of pediatrics, Yale University, New Haven, Conn., for contributions on disturbances in water and electrolytes, the American Academy of Pediatrics.

Paul Gyorgy, professor of clinical pediatrics, University of Pennsylvania, Philadelphia, for research on the nutrients contained in milk, the American Institute of Nutrition.

Frances A. Johnston, Ph.D., associate professor of food and nutrition, Cornell University, New York, for investigations in the field of iron and calcium metabolism and biochemistry, the American Home Economics Association.

Thomas L. McMeekin, Ph.D., of the Eastern Regional Research Laboratory, U. S. Department of Agriculture, Philadelphia, for contributions to chemistry and utilization of milk proteins, the American Chemical Society.

Cancer Conference in Wichita.—The fourth annual Mid-West Cancer Conference will be held at the Broadview Hotel in Wichita, Kan., April 3-4. Speakers from outside the Midwest include:

Edward D. Churchill, Boston, Carcinoma of the Lung.

John S. Ladue, New York, Risk Problems in Cancer Surgery.

Lowell S. Goin, Los Angeles, Role of Radiation Therapy in Treatment of Malignant Disease.

Joe V. Meigs, Boston, Diagnosis and Treatment of Cancer of Cervix.

Gould A. Andrews, Oak Ridge, Tenn., Radioactive Iodine in the Management of Thyroid Carcinoma.

At the informal dinner meeting on Thursday Dr. Charles S. Cameron, medical and scientific director of the American Cancer Society, will speak on "Program and Services of the American Cancer Society." There will be roundtable luncheons and informal discussion periods in which all guest speakers will participate. The conference is sponsored by the Kansas Division of

MEETINGS

the American Cancer Society and the program is arranged by the Committee on the Control of Cancer of the Kansas Medical Society. Correspondence should be addressed to the conference, 501-511 Brown Bldg., Wichita, Kan.

Airplane Accidents and Age of Pilots.—A study of 59 fatal airline accidents in the last 15 years shows no evidence that older pilots are less safe in an emergency than their younger colleagues, according to Ross A. McFarland, Ph.D., a professor at the Harvard University School of Public Health and medical co-ordinator of Pan American World Airways. Dr. McFarland gave this finding Feb. 23 at a meeting of the Airline Medical Directors Association at Randolph Field headquarters of the Air Force School of Aviation Medicine in Texas. Most of the fatal crashes occurred in the first three hours of flight, and so fatigue was not a factor, as you might expect if older pilots were to blame, said Dr. McFarland. About 1,400 flyers between 40 and 50 years of age now hold airline certificates. Some symptoms of advancing years can be safely corrected. Wearing glasses, for instance, is not considered a reason in itself to ground an airline pilot, if the necessary correction is not extreme. Veteran pilots claim that their ability to foresee emergencies and to plan a course of action for themselves in advance is more valuable than the youthful pilot's swift reactions when the emergency occurs.

FOREIGN

Progress in Malaria Control in Northern India.—Following the success of malaria control operations launched about two years ago in Northern India, the World Health Organization has suggested to the Upper Pradesh Government undertaking a low-cost campaign to banish malaria throughout the state within the next few years. Throughout 1,750 square miles of the Terai a stable population of 150,000 plus a floating (winter) population of 45,000 is at present receiving almost 100% protection from malaria through DDT spraying of 1,300 villages by a team recruited by the government, operating under the leadership of WHO malaria expert from Greece, and using supplies furnished mostly by the United Nations Children's Emergency Fund. Microscopic examination revealed that, before spraying started, from one-half to three-fourths of infants in the area got malaria during their first year of life. After the first year of DDT spraying the figure dropped to 2.6% while after the second year, no babies were becoming infected. Requests are now pouring in to the team's headquarters for the expansion of control operation to neighboring malarial areas.

In addition to the collection of infant blood-slides, nurses give advice to mothers and treat children for minor ailments. Maternal and child health centers have opened in several parts of the area. At the Haldwani center, for instance, about 450 mothers attend each month for prenatal and postnatal advice and treatment.

DEATHS IN OTHER COUNTRIES

Maj. Gen. Ralph Ainsworth, formerly commandant and director of studies at the Royal Army Medical College, died in London Jan. 27, aged 76. He was knighted in 1946 for his activities as director of medical services of the Joint War Organization of the British Red Cross Society and Order of St. John. —**Carlos Bonorino Udaondo**, Buenos Aires, several times president of the National Academy of Medicine, dean and honorary professor of the Faculty of Medicine, University of Buenos Aires, died Nov. 15, aged 67. He was a delegate to medical congresses in Latin America and in Europe, serving as president of the First Pan-American Congress of Gastroenterology. He was the founder of the Society of Gastroenterology and Nutrition of Buenos Aires.

CORRECTION

Drug Prophylaxis of Amebiasis.—In table 2 of the article on drug prophylaxis of amebiasis by Berberian and co-workers (*J. A. M. A.* 148:700 [March 1] 1952), the words "infected" and "not infected" were incorrectly inserted under the heading Medication Regimen. In these two columns, a plus sign should be substituted for the word "infected" and a minus sign for the words "not infected."

- AERO MEDICAL ASSOCIATION, Hotel Statler, Washington, D. C., March 17-19. Dr. Thomas H. Sutherland, 214 South State St., Marion, Ohio, Secretary.
- ALABAMA, MEDICAL ASSOCIATION OF THE STATE OF, Montgomery, April 17-19. Dr. Douglas L. Cannon, 519 Dexter Ave., Montgomery, Secretary.
- AMERICAN ACADEMY OF GENERAL PRACTICE, Atlantic City, N. J., March 24-27. Mr. Mac F. Cahal, 406 West 34th St., Kansas City 2, Mo., Executive Secretary.
- AMERICAN ACADEMY OF NEUROLOGY, Brown Hotel, Louisville, Ky., Apr. 24-25. Dr. Francis M. Forster, 3800 Reservoir Rd. N.W., Washington, D. C., Secretary.
- AMERICAN ACADEMY OF OBSTETRICS AND GYNECOLOGY, Cincinnati, April 1. Dr. Ralph A. Reis, 116 South Michigan Boulevard, Chicago 3, Secretary.
- AMERICAN ASSOCIATION OF ANATOMISTS, Providence, R. I., March 19-21. Dr. Normand L. Hoerr, 2109 Adelbert Road, Cleveland 6, Secretary.
- AMERICAN ASSOCIATION OF IMMUNOLOGISTS, New York, April 14. Dr. John Y. Sugg, 1300 York Ave., New York, Secretary.
- AMERICAN ASSOCIATION OF PATHOLOGISTS AND BACTERIOLOGISTS, New York, April 10-12. Dr. Alan R. Moritz, 2085 Adelbert Road, Cleveland 6, Secretary.
- AMERICAN ASSOCIATION OF RAILWAY SURGEONS, Drake Hotel, Chicago, April 1-3. Dr. Chester C. Guy, 5800 Stony Island Ave., Chicago 37, Secretary.
- AMERICAN COLLEGE OF ALLERGISTS, William Penn Hotel, Pittsburgh, April 7-9. Dr. Fred W. Wittich, 401 LaSalle Medical Bldg., Minneapolis 2, Secretary.
- AMERICAN COLLEGE OF PHYSICIANS, Cleveland, April 21-25. Mr. E. R. Loveland, 4200 Pine St., Philadelphia 4, Executive Secretary.
- AMERICAN COLLEGE OF SURGEONS, SECTIONAL MEETINGS:
Minneapolis, Radisson Hotel, March 24-26. Dr. Harvey Nelson, 78 South 9th St., Minneapolis 2, Chairman.
Tucson, Ariz., Pioneer Hotel, April 7-9. Dr. Meade Clyne, 110 South Scott St., Tucson, Chairman.
Vancouver, B. C., Vancouver Hotel, March 31-April 4. Dr. J. Russell Neilson, 925 West Georgia St., Vancouver, B. C., Chairman.
- AMERICAN CONGRESS ON OBSTETRICS AND GYNECOLOGY, Netherlands-Plaza Hotel, Cincinnati, March 31-April 4. Dr. Luella E. Nadelhoffer, 116 South Michigan Ave., Chicago 3, Secretary.
- AMERICAN DERMATOLOGICAL ASSOCIATION, Broadmoor Hotel, Colorado Springs, Colo., Apr. 23-26. Dr. Louis A. Brunsting, 102 Second Ave. S.W., Rochester, Minn., Secretary.
- AMERICAN GASTRO-ENTEROLOGICAL ASSOCIATION, Hotel Claridge, Atlantic City, N. J., May 2-3. Dr. Dwight L. Wilbur, 655 Sutter St., San Francisco 2, Secretary.
- AMERICAN GASTROSCOPIC SOCIETY, Hotel Claridge, Atlantic City, N. J., May 2-3. Dr. H. Marvin Pollard, University Hospital, Ann Arbor, Mich., Secretary.
- AMERICAN GOUTER ASSOCIATION, Chase Hotel, St. Louis, May 1-3. Dr. George C. Shivers, 100 East St. Vrain St., Colorado Springs, Colo., Secretary.
- AMERICAN HEART ASSOCIATION, Hotel Statler, Cleveland, April 17-20. Dr. William H. Bunn, 1775 Broadway, New York 19, Secretary.
- AMERICAN PSYCHOSOMATIC SOCIETY, The Drake, Chicago, March 29-30. Dr. Frederick C. Redlich, 551 Madison Avenue, New York 22, Secretary.
- AMERICAN SOCIETY FOR EXPERIMENTAL PATHOLOGY, New York, April 14-18. Dr. Russell L. Holman, 1542 Tulane Ave., New Orleans 12, Secretary.
- AMERICAN SOCIETY FOR PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, Hotel Statler, New York, April 14-18. Dr. Carl C. Pfeiffer, 1835 W. Polk St., Chicago 12, Secretary.
- AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, New York, April 14-18. Dr. Elmer H. Stotz, 260 Crittenden Blvd., Rochester, N. Y., Secretary.
- AMERICAN SURGICAL ASSOCIATION, White Sulphur Springs, W. Va., Apr. 16-18. Dr. Nathan A. Womack, University Hospitals, Iowa City, Secretary.
- AMERICAN VENEREAL DISEASE ASSOCIATION, Washington, D. C., May 1-2. Dr. William L. Fleming, 750 Harrison Ave., Boston 18, Secretary.
- ARIZONA MEDICAL ASSOCIATION, Phoenix, April 30-May 3. Dr. Frank J. Milloy, 15 E. Monroe St., Phoenix, Secretary.
- ARKANSAS MEDICAL SOCIETY, Little Rock, April 21-23. Dr. William R. Brooksher, 215 Kelley Bldg., Fort Smith, Secretary.
- CALIFORNIA MEDICAL ASSOCIATION, Biltmore Hotel, Los Angeles, April 27-30. Dr. Albert C. Daniels, 450 Sutter St., San Francisco 8, Secretary.
- CONNECTICUT STATE MEDICAL SOCIETY, Hartford, April 29-May 1. Dr. Creighton Barker, 160 St. Ronan Street, New Haven, Secretary.
- DALLAS SOUTHERN CLINICAL SOCIETY, Dallas, Texas, March 17-20. Dr. Earl L. Loftis, 433 Medical Arts Bldg., Dallas 1, Secretary.
- FLORIDA MEDICAL ASSOCIATION, Hollywood, April 27-30. Dr. Samuel M. Day, P. O. Box 1018, Jacksonville, Secretary.
- HAWAII TERRITORIAL MEDICAL ASSOCIATION, Honolulu, May 1-4. Dr. I. L. Tilden, 510 S. Beretania St., Honolulu 13, Secretary.
- INDUSTRIAL MEDICAL ASSOCIATION, Cincinnati, April 21-24. Dr. Edward C. Holmblad, 28 E. Jackson Blvd., Chicago 4, Managing Director.
- IOWA STATE MEDICAL SOCIETY, Des Moines, April 28-30. Dr. Allan B. Phillips, 406 Sixth Avenue, Des Moines 9, Secretary.
- JOHN A. ANDREW CLINICAL SOCIETY, Memorial Hospital, Tuskegee Institute, Ala., April 6-12. Dr. Eugene H. Dibble Jr., Memorial Hospital, Tuskegee Institute, Secretary.
- KANSAS MEDICAL SOCIETY, Town House, Kansas City, April 27-May 1. Dr. Dale D. Vermillion, 512 New England Bldg., Topeka, Secretary.

LOUISIANA STATE MEDICAL SOCIETY, Shreveport, April 28-30. Dr. C. Grenes Cole, 1430 Tulane Ave., New Orleans 12, Secretary.

MARYLAND, MEDICAL AND SURGICAL FACULTY OF THE STATE OF, Baltimore, April 28-30. Dr. George H. Yeager, 1211 Cathedral St., Baltimore 1, Secretary.

MID-CONTINENT PSYCHIATRIC ASSOCIATION, President Hotel, Kansas City, Mo., April 26-27. Dr. Paul Hines, 2625 W. Pasco, Kansas City, Mo., Secretary.

MISSOURI STATE MEDICAL ASSOCIATION, Hotel Jefferson, St. Louis, March 30-April 2. Dr. H. E. Petersen, 634 North Grand Blvd., St. Louis 3, Secretary.

NORTH PACIFIC SOCIETY OF INTERNAL MEDICINE, Portland, Ore., March 22. Dr. R. L. King, 1115 Terry Ave., Seattle 1, Secretary.

PIEDMONT PROCTOLOGIC SOCIETY, Charlotte, N. C., March 29-30. Dr. B. Richard Jackson, 224 Hillsboro St., Raleigh, N. C., Secretary.

POST GRADUATE INSTITUTE OF THE PHILADELPHIA COUNTY MEDICAL SOCIETY, Bellevue-Stratford Hotel, Philadelphia, April 1-4. Dr. Thomas M. Durant, 301 South 21st St., Philadelphia 3, Director.

SOCIETY OF AMERICAN BACTERIOLOGISTS, Hotel Statler, Boston, April 27-May 1. Dr. Henry W. Scherp, 260 Crittenden Blvd., Rochester 20, N. Y., Secretary.

SOUTHEASTERN ALLERGY ASSOCIATION, Bon Air Hotel, Augusta, Ga., March 21-22. Dr. Katharine B. MacInnis, 1515 Bull St., Columbia 49, S. C., Secretary.

SOUTHEASTERN SECTION, AMERICAN UROLOGICAL ASSOCIATION, Boca Raton, Fla., April 2-5. Dr. Russell B. Carson, Sweet Bldg., Fort Lauderdale, Fla., Secretary.

SOUTHEASTERN SURGICAL CONGRESS, Biltmore Hotel, Atlanta, Ga., March 10-14. Dr. Benjamin J. Beasley, 701 Hurt Bldg., Atlanta 3, Ga., Secretary.

TENNESSEE STATE MEDICAL ASSOCIATION, Andrew Johnson Hotel, Knoxville, April 7-9. Mr. V. O. Foster, 504 Doctors Bldg., Nashville 3, Executive Secretary.

UNITED STATES-MEXICO BORDER PUBLIC HEALTH ASSOCIATION, Monterrey, Nuevo Leon, Mexico, March 17-19. Dr. J. C. Ellington, 314 U. S. Court House, El Paso, Texas, Secretary.

WESTERN ASSOCIATION OF INDUSTRIAL PHYSICIANS AND SURGEONS, Biltmore Hotel, Los Angeles, April 26. Dr. David D. Holaday, American Can Company, Third and 20th Sts., San Francisco 7, Secretary.

INTERNATIONAL

AUSTRALASIAN MEDICAL CONGRESS, Melbourne Victoria, Australia, Aug. 22-30. Dr. C. H. Dickson, Medical Society Hall, 426 Albert St., East Melbourne, Victoria, Australia, Hon. General Secretary.

COMMONWEALTH AND EMPIRE HEALTH AND TUBERCULOSIS CONFERENCE, Central Hall, London, England, July 8-13. Dr. J. H. Harley Williams, Tavistock House North, Tavistock Sq., London, W.C.1, England, Secretary General.

CONGRESS OF THE INTERNATIONAL DIABETES FEDERATION, Leyden, Netherlands, July 7-12. Dr. F. Gerritzen, 33, Prinsegracht, The Hague, Netherlands, Secretary.

EUROPEAN CONGRESS OF CARDIOLOGY, University of London, Bloomsbury, W.C.1, England, Sept. 10-12. Dr. K. Shirley Smith, 35 Wimpole St., London, W.1, England, Secretary.

EUROPEAN SOCIETY OF CARDIOVASCULAR SURGERY, Strasbourg, France, Oct. 3-4. Sir James Learmonth, Department of Surgery, University New Buildings, Edinburgh 8, Scotland.

INTERAMERICAN CARDIOLOGICAL CONGRESS, Buenos Aires, Argentina, Aug. 31-Sept. 7. Dr. Blas Moia, Larrea 1132, Buenos Aires, Argentina, Secretary-General.

INTER-AMERICAN CONGRESS OF PUBLIC HEALTH, Havana, Cuba, Sept. 27-Oct. 1. Pan-American Sanitary Bureau, 2001 Connecticut Ave., Washington, D. C.

INTER-AMERICAN CONGRESS OF RADIOLOGY, Mexico City, Mexico, Nov. 2-6. Dr. Guido Torres Martinez, Marsella No. 11, Mexico, D.F., Secretary-General.

INTERNATIONAL COLLEGE OF SURGEONS, Madrid, Spain, May 20-24. Dr. Max Thorek, 850 West Irving Park Road, Chicago, Ill., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF COMPARATIVE PATHOLOGY, Madrid, Spain, May 4-11. Prof. Carda-Aparici, Calle Fernando VI.8, Madrid, Spain, Secretary.

INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY, London, England, July 21-26. Dr. Gordon B. Mitchell-Heggs, 5, Lisle St., London, W.C.2, England, General Secretary.

INTERNATIONAL CONGRESS ON DIABETES, Leyden, The Netherlands, July 7-12. Dr. F. Gerritzen, 33, Prinsegracht, The Hague, Netherlands.

INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST, Rio de Janeiro, Brazil, Aug. 24-30. Mr. Murray Kornfeld, 112 East Chestnut St., Chicago 11, Illinois, Executive Secretary.

INTERNATIONAL CONGRESS OF HAEMATOLOGY, Mar del Plata, Argentina, Sept. 21-26. Dr. Carlos Reussi, Anchorena 1710, Buenos Aires, Argentina, Secretary.

INTERNATIONAL CONGRESS OF HEALTH TECHNICIANS, Palais de la Mutualite, Paris, France, June 9-14. Secretariat General, 6 Square Desaix, Paris XV, France.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Friends House, London, N.W.1, Eng. Sept. 15-18. Sir Harold Boldero, 12 Pall Mall East, London, S.W.1, England, Secretary.

INTERNATIONAL CONGRESS ON MEDICAL RECORDS, London, England, Sept. 7-12. Miss Gwen Perkins, 120 C Street S.E., Washington, D. C., Chairman.

INTERNATIONAL CONGRESS ON NEUROPATHOLOGY, Rome, Italy, Sept. 8-13. Dr. Armando Ferraro, 722 W. 168th St., New York, N. Y., U. S. A., Secretary General.

INTERNATIONAL CONGRESS OF OTO-NEURO-OPTHALMOLOGY, Lisbon and Estoril, Portugal, April 22-26. Prof. Diogo Furtado, Servico de Neurologia, Hospital dos Capuchos, Lisbon, Portugal, General Secretary.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE, London, England, July 14-19. Dr. A. C. Boyle, 45, Lincoln's Inn Fields, London, W.C.2, England, Hon. Secretary.

INTERNATIONAL CONGRESS FOR THERMALISM AND CLIMATOTHALASSOTHERAPY, Nice-Cannes, France, April 3-8.

INTERNATIONAL SOCIETY OF GEOGRAPHIC PATHOLOGY, Liège, Belgium, July 15-18. Dr. Fred C. Roulet, Habelstr. 24, Basel, Switzerland, Secretary General.

INTERNATIONAL UNION AGAINST TUBERCULOSIS, Rio de Janeiro, Brazil, Aug. 24-27. Prof. Etienne Bernard, 66 Blvd. St. Michel, Paris 6e, France, Secretary-General.

NEURORADIOLOGIC SYMPOSIUM, Stockholm, Sweden, Sept. 17-20. Docent Ake Lindbom, Symposium Neuroradiologicum, Serafimerlasarettet, Stockholm K., Sweden, Secretary.

PAN-AMERICAN CONGRESS OF GASTROENTEROLOGY, Mexico City, D.F., May 11-17. Dr. R. Flores-Lopez, Calle Dr. Balmis, No. 148, Mexico City, D.F., Secretary.

PAN-EUROPEAN CONGRESS OF GASTROENTEROLOGY, Bologna, Florence and Rome, Italy, April 20-26. Prof. Guido Bassi, Policlinic of St. Orsola, Bologna, Italy, Secretary.

WORLD MEDICAL ASSOCIATION, Athens, Greece, Oct. 12-16. Dr. Louis H. Bauer, 2 East 103d St., New York 29, N. Y., Secretary General.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Part II*, April 21-22; *Parts I and II*, June 16-18 or June 23-25; *Part I*, September. All centers where there are five or more candidates. Exec. Sec., Dr. John P. Hubbard, 225 S. 15th St., Philadelphia 2.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: Various Locations, July 18. Final date for filing application was Jan. 18. Sec., Dr. C. B. Hickcox, 80 Seymour St., Hartford 15.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written*. Various centers. March 1952. *Oral*. Chicago, May 1952. Final date for filing application was Feb. 1, 1952. Candidates for these tests must have completed three years of approved training prior to July 1, 1952. Sec., Dr. George M. Lewis, 66 E. 66th St., New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written*. Various centers and overseas, Oct. 20. Closing date for the acceptance of applications for the written examination will be May 1. *Oral*. Cleveland, April 17-19; Chicago, June 5-7, San Francisco, September or October; New York City, November or December. Subspecialty: Gastroenterology. *Examination*. Chicago, June 7. Exec. Sec.-Treas., Dr. William A. Wertell, 1 West Main Street, Madison 3.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral*. Chicago, May 1952. Final date for filing applications for the May 1952 examination was Jan. 1. Sec., Dr. W. J. German, 789 Howard Ave., New Haven 4, Conn.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Oral*. Chicago, June 9-13, 1952. Final date for filing application was Feb. 1, 1952. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Practical*. Philadelphia, May 29-June 3; Chicago, Oct. 6-10 and New York City, June 6-10, 1953. Sec., Dr. Edwin B. Dunphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part I*. San Francisco and Washington, D. C., April 25-26. Sec., Dr. Harold A. Sofield, 122 South Michigan Ave., Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY. Toronto, May 13-17; Chicago, Oct. 6-10. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PEDIATRICS: *Oral*. St. Louis, Mo., Mar. 21-23; Washington, D. C., May 2-4; San Francisco, late June; Chicago, October and Boston, late November. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION: *Parts I and II*. Chicago. June 8 and 9. Sec., Dr. Robert L. Bennett, Georgia Warm Springs Foundation, Warm Springs, Ga.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral and Written*. St. Louis, May 17-19. Sec., Dr. Bradford Cannon, 4647 Pershing Ave., St. Louis 8.

AMERICAN BOARD OF PREVENTIVE MEDICINE AND PUBLIC HEALTH. *Written*. Berkeley, Calif., Minneapolis, New Orleans and Baltimore. April 18. Sec., Dr. Ernest L. Stebbins, 615 N. Wolfe St., Baltimore.

AMERICAN BOARD OF PROCTOLOGY. *Part I*. Kansas City, Minneapolis, Philadelphia and San Francisco. May 3. Examination includes both oral and written examinations in the basic sciences. *Dates and places tentative*. Sec., Dr. Louis A. Buie, 102-110 2d Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: Chicago, June 13-14. Final date for filing applications was March 15. New York City, Dec. 15-16. Final date for filing applications is Sept. 15. Sec.-Treas., Dr. David A. Boyd, Jr., 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Oral*. Spring 1952. Final date for filing application was Dec. 31. Sec., Dr. B. R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written*. Various Centers. March 1952. Final date for filing application was Dec. 1, 1951. The following written examination will be given in October 1952. Sec., Dr. J. Stewart Rodman, 225 S. 15th St., Philadelphia.

DEATHS

Kennedy, Foster ☉ New York; born in Belfast, Ireland, Feb. 7, 1884; National University of Ireland, 1906; professor of clinical medicine (neurology) Cornell University Medical College; member and past president of the American Neurological Association and the New York Neurological Society; formerly recording secretary of the New York Academy of Medicine; trustee, formerly chairman of the board of trustees, and past president of the Association for Research in Nervous and Mental Diseases; member of the American Psychiatric Association and American Psychopathic Association; fellow of the Royal Society of Edinburgh and Royal Society of Medicine, London; honorary member of the Neurological Society of Paris, Hungary, Cuba, Mexico, and Sweden; chairman of the committee on neuropsychiatry of the National Research Council, Washington, D. C.; served as chairman of the Federal Medical Commission on Ellis Island; during World War I served with the French and British armies, physician-in-chief of a French military hospital and a major in the Royal Army Medical Corps; affiliated with Neurological Institute, Bellevue Hospital, New York Hospital, Lenox Hill Hospital and Woman's Hospital; consulting neurologist to Monmouth Memorial Hospital in Long Branch, N. J., and Nassau Hospital, Mineola; in 1929 one of seven appointed to the New York City Noise Abatement Committee; in 1937 the Order of Merit of Carlos Finlay was conferred on him; decorated Chevalier of the Legion of Honor of France; died in Bellevue Hospital Jan. 7, aged 67.

Brunk, Andrew S. ☉ Detroit; born in 1884; Cleveland Homeopathic Medical College, 1909; treasurer and past president of the Michigan State Medical Society and since 1930 member of the council and of its executive committee from 1939 to 1945; past president of the Wayne County Medical Society and for five years served on the board of trustees; a founder, first president, and member of the board of trustees and of the executive committee, Michigan Health Council; served on the board of directors of Michigan Medical Service for more than 10 years; member of the Blue Shield Board of Directors from 1940 until his death; one of the founders and first president of the Conference of Presidents and Other Officers of State Medical Associations; one of the founders of the Michigan Foundation for Medical and Health Education, Inc.; member of the board of directors of Michigan Hospital Service (Blue Cross) and served on its executive committee from 1939 to 1948; honorary member of the Colorado State Medical Society; director of Martin Place Hospital, which he established in 1930; chief surgeon for the Southern Pacific Railroad in La Junta, Colo., from 1911 to 1924; died in San Antonio, Texas, Feb. 3, aged 67.

Carson, Archibald Irwin, Cincinnati; born in Cincinnati March 10, 1864; Miami Medical College, Cincinnati, 1889; professor emeritus of clinical surgery at University of Cincinnati College of Medicine; fellow of the American College of Surgeons; served as a member and president of the city board of health; consulting surgeon, Cincinnati General Hospital; served as a trustee of Christ Hospital; past president of the Cincinnati Society of Natural History; in 1885 organized and was captain of the University of Cincinnati's first football team; the home grounds of the Cincinnati Bearcats are named Carson Field in his honor; formerly librarian of the Cincinnati Academy of Medicine; died in Christ Hospital Dec. 20, aged 87, of lobar pneumonia and granuloma of the right lung.

Carmichael, Francis Abbott Sr. ☉ Kansas City, Mo.; born in Rockford, Ill., Oct. 28, 1871; Northwestern University Medical School, Chicago, 1904; an Associate Fellow of the American Medical Association and member of its House of Delegates in 1923 and from 1926 to 1929; member of the American Psychiatric Association; past president of the Kansas Medical Society; specialist certified by the American Board of Psychiatry and Neurology; served during World War I; resigned in 1926 as superintendent of the Osawatimic State Hospital in Osawatimic

after 23 years' service; later appointed chief clinical adviser of the six state hospitals in Missouri; died in St. Mary's Hospital Jan. 21, aged 80, of heart disease.

Brutsch, George Charles, Minneapolis; University of Minnesota Medical School, Minneapolis, 1931; member of the American Medical Association; served during World War II; died in Deaconess Hospital Nov. 9, aged 51, of coronary thrombosis.

Burton, Oscar Augustus ☉ Brattleboro, Vt.; Rush Medical College, Chicago, 1898; town physician and health officer for Brattleboro; on the staff of the Brattleboro Memorial Hospital; died Jan. 1, aged 81, of acute myocardial infarction.

Bushman, Louis Bernard Jr., Omaha; University of Nebraska College of Medicine, Omaha, 1942; served during World War II; died Dec. 18, aged 34, of coronary disease.

Dredge, Verly H., Cleveland Heights, Ohio; Western Reserve University School of Medicine, Cleveland, 1921; affiliated with University Hospitals, Huron Road Hospital, and St. Luke's Hospital, Cleveland, where he died Dec. 11, aged 66, of myocardial infarction.

Fauman, David Haymes ☉ Detroit; University of Toronto Faculty of Medicine, Toronto, Canada, 1915; died in Harper Hospital Dec. 31, aged 60, of cardiovascular disease.

Fowler, Richard Mark, Atlantic City, N. J.; University of Pittsburgh School of Medicine, 1913; on the staff of the Atlantic City Hospital; died Nov. 13, aged 67, of cerebral thrombosis.

Handford, William Bancroft ☉ Caldwell, Idaho; University of Oregon Medical School, Portland, 1931; formerly secretary-treasurer of the Idaho State Medical Association; served during World War II; died Dec. 24, aged 46, as the result of a fall.

Highsmith, Lewis Langston, Kingsport, Tenn.; University College of Medicine, Richmond, 1912; on the staff of Holston Valley Community Hospital; died in Tucker Hospital, Richmond, Va., Dec. 30, aged 68, of arteriosclerotic heart disease.

Kaplan, Emanuel Mandel, Chicago; Rush Medical College, Chicago, 1921; member of the American Medical Association; assistant professor of surgery, Chicago Medical School; on the staffs of Mount Sinai, Michael Reese, and University hospitals; died Dec. 29, aged 55, of rheumatic and hypertensive heart disease.

Krigbaum, Roy Edmund ☉ Columbus, Ohio; Ohio State University College of Medicine, Columbus, 1919; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the American College of Surgeons; past president of the Columbus Obstetrical and Gynecological Society; at one time on the faculty of his alma mater; for many years chief-of-staff of St. Ann's Maternity Hospital; on the surgery courtesy staffs of St. Francis and St. Anthony hospitals; died Dec. 18, aged 58, of cerebral hemorrhage.

Langdon, John Frederick, Omaha; John A. Creighton Medical College, Omaha, 1906; member of the American Medical Association; associate professor of surgery at his alma mater; fellow of the American College of Surgeons; member of the founders group of the American Board of Surgery; past president of the Douglas County Medical Society; on the staff of St. Catherine's Hospital and Creighton Memorial St. Joseph's Hospital, where he died Dec. 17, aged 69, of coronary occlusion.

Leigh, Octa Charles Jr., New York; Harvard Medical School, Boston, 1934; member of the American Medical Association, American Association for the Advancement of Science, and Society of University Surgeons; certified by the American Board of Surgery; served during World War II; on the staff of the Presbyterian Hospital; on the part time staff of the department of surgery, Columbia University College of Physicians and Surgeons; died suddenly, Dec. 26, aged 46, of coronary thrombosis.

Leshner, Charles Byron, Camden, N. J.; University of Pennsylvania Department of Medicine, Philadelphia, 1908; formerly a medical missionary in China; affiliated with Cooper Hospital, where he died Nov. 8, aged 73, of coronary occlusion.

Lovell, John Frederick, Irvington, N. J.; Boston University School of Medicine, 1908; member of the American Medical Association, American Society of Anesthesiologists, and the Radiological Society of North America; served as mayor, town commissioner, director of the department of public affairs, and member of the board of education; at one time affiliated with the U. S. Public Health Service; on the staff of Irvington General Hospital; died in Springfield Dec. 29, aged 65, of embolism and hypertensive cardiovascular disease.

McElhinney, Philip Paul Bliss ☉ Long Beach, Calif.; Jefferson Medical College of Philadelphia, 1920; certified by the American Board of Urology; member of the American Urological Association; fellow of the American College of Surgeons; served in the Pacific during World War II; on the staffs of Seaside, St. Mary's and Community hospitals; died Dec. 15, aged 58, of coronary occlusion.

Manney, Willis Edwin ☉ Wadsworth, Kan.; Baylor University College of Medicine, Dallas, 1928; member of the American Psychiatric Association; served during World War II; affiliated with the Veterans Administration since 1931; medical officer of the Veterans Administration Center; appointed manager of the new Veterans Administration Hospital in Kansas City, Mo., to begin Jan. 1; died Dec. 7, aged 46, of carcinoma.

Marquart, Carl Albert, Crestline, Ohio; Cleveland University of Medicine and Surgery, 1895; past president of the Crawford County Medical Society; formerly served as county coroner and health officer of Crestline; for many years member of the board of education; affiliated with Crestline Emergency Hospital; surgeon for the Pennsylvania Railroad; died Dec. 20, aged 77, of a heart attack.

Maxon, Oscar Fritzallen, Springfield, Ill.; Rush Medical College, Chicago, 1900; member of the American Medical Association; at one time medical director of the Franklin Life Insurance Company; died in St. John's Hospital Dec. 24, aged 78, of coronary thrombosis with myocardial infarction.

Miles, George Albert ☉ Somerville, Mass.; Long Island College Hospital, Brooklyn, 1891; an Associate Fellow of the American Medical Association; for many years on the staff of Somerville Hospital, where he died Dec. 15, aged 87, of pneumonia.

Minor, Ward Allen ☉ Utica, N. Y.; Eclectic Medical College of the City of New York, 1890; Baltimore University School of Medicine, 1894; also a pharmacist; served during World War I; formerly county health officer; member of the staff of Faxon Hospital; director of the Citizens National Bank of Oneonta, which he helped organize; died December 10, aged 84, of chronic myocarditis and diabetes mellitus.

Moore, Paul Dame, Sacramento, Ky.; Louisville and Hospital Medical College, Louisville, Ky., 1908; member of the American Medical Association; died Dec. 21, aged 70.

Munro, Alonzo T., Kalispell, Mont.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1897; formerly a member of the state board of medical examiners; served on the staff of Kalispell General Hospital; died Dec. 18, aged 76, of cardiorenal disease.

Newman, Harold Hastings ☉ Salisbury, N. C.; Johns Hopkins University School of Medicine, Baltimore, 1913; fellow of the American College of Surgeons; on the staff of Rowan Memorial Hospital; died Dec. 24, aged 62, of coronary thrombosis.

Niblick, James Stewart ☉ East Chicago, Ind.; Chicago College of Medicine and Surgery, 1917; fellow of the American College of Physicians; member of the Industrial Medical Association; health officer of East Chicago; past president of the Lake County Medical Society; affiliated with St. Mary's Mercy Hospital in Gary and St. Catherine's Hospital; head physician for the Inland Steel Company and the Youngstown Sheet and Tube Company; died in St. Catherine's Hospital Dec. 27, aged 56, of coronary heart disease.

Norton, Walter Abell, Savannah, Ga.; Atlanta College of Physicians and Surgeons, 1903; member of the American Medical Association and Southeastern Surgical Congress; fellow of the American College of Surgeons; served during World War I; lieutenant colonel in the medical reserve corps of the U. S. Army; on the staff of Warren A. Candler Hospital; surgeon for American Can and Savannah Electric and Power Companies; died Dec. 3, aged 70.

Oliver, Harry Reeves ☉ San Francisco; Cooper Medical College, San Francisco, 1898; formerly associated with the department of pathology at his alma mater; served on the faculty of Stanford University School of Medicine; an officer during World War I; affiliated with Mount Zion Hospital, St. Luke's Hospital, and St. Mary's Hospital, where he died Dec. 26, aged 79, of carcinoma of the prostate.

Palmer, William Gaston, Cleveland; Harvard Medical School, Boston, 1947; resident, University Hospitals; died Nov. 25, aged 27.

Parks, William Alvah ☉ Akron, Ohio; Rush Medical College, Chicago, 1909; member of the International College of Surgeons; fellow of the American College of Surgeons; past president of the Summit County Medical Society; affiliated with Akron City and St. Thomas hospitals; died Oct. 12, aged 70, of pneumonia.

Reed, Elias Alfred ☉ Brooklyn; Long Island College Hospital, Brooklyn, 1919; member of the American Psychiatric Association; specialist certified by the American Board of Psychiatry and Neurology; affiliated with the Jewish Hospital for many years; chief psychiatrist and director of the Brooklyn Child Guidance Clinic; died Dec. 27, aged 56, of carcinoma of the rectum.

Robinson, Bradbury J., Farmington, Mo.; Marion-Sims College of Medicine, St. Louis, 1892; member of the American Medical Association; died Dec. 2, aged 84, of pneumonia.

Robinson, Ethelred Fisher, Denver; Chicago College of Medicine and Surgery, 1909; member of the American Medical Association; died Dec. 10, aged 71.

Ross, Leo M., Newark, Ohio; Eclectic Medical Institute, Cincinnati, 1898; died in Newark City Hospital Nov. 15, aged 81, of cerebral embolism.

Rowell, James Frederick, Lawton, Okla.; Hahnemann Medical College and Hospital of Philadelphia, 1895; died in Oklahoma City Nov. 6, aged 77, of a cerebral vascular accident and hypertension.

Ryder, Delano Richmond ☉ Fall River, Mass.; University of Vermont College of Medicine, Burlington, 1904; member of the American Academy of Ophthalmology and Otolaryngology and the New England Otolaryngological Society; fellow of the American College of Surgeons; affiliated with Truesdale Hospital; died in Barrington, R. I., Dec. 19, aged 78, of heart disease.

Schaffer, Herman Armin, St. Albans, N. Y.; Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest, Hungary, 1911; member of the American Medical Association; for many years on the staff of Lenox Hill Hospital, died recently, aged 64.

Siev, Samuel, Queens Village, N. Y.; Albertus-Universität Medizinische Fakultät, Königsberg, Germany, 1923; member of the American Medical Association; died Nov. 24, aged 55.

Sterling, John Scott, Jerome, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1903; died Nov. 29, aged 74.

Stranberg, Walter Leonard ☉ Wauwatosa, Wis.; Northwestern University Medical School, Chicago, 1911; served during World War I; affiliated with Misericordia Hospital and Evangelical Deaconess Hospital, Milwaukee, where he died Oct. 9, aged 65, of ruptured aortic aneurysm.

Williams, Lois Flint Durkee, Fort Pierce, Fla.; Tennessee Medical College, Knoxville, 1908; died Nov. 18, aged 68, of nephritis.

GOVERNMENT SERVICES

ARMY

Cineplastic Case History Unit.—Cineplastic surgery is a method of providing a skin-lined tunnel through a muscle adjacent to an amputation stump to permit harnessing of the muscle for operation of an artificial hand. A new unit has been established at Walter Reed Army Medical Center to record studies of amputee patients from the time they are found eligible for cineplastic surgery until they leave the hospital. Establishment of this unit at the prosthetics research laboratory rounds out a program aimed at providing a concerted effort in the field of cineplastic surgery. The over-all program at Walter Reed Army Medical Center covers research in surgical procedures, development of special muscle-building exercises, the fitting of artificial hands and hooks designed particularly for the cineplastic amputee, training in the use of artificial devices, and establishment of criteria for future improvements in these prostheses.

The case history unit has a two-fold purpose. It will acquaint the amputee with the ultimate functional possibilities of his artificial hand and provide a clinical record of such amputees for the continuance of research to develop more precise hands and hooks particularly adaptable to muscular control. The unit testing engineer, Lt. Albert Clark, works under the supervision of Dr. Fred Leonard, 8720 Colesville Road, Silver Spring, Md., chief of the laboratory's testing branch. Lieutenant Clark is a cineplastic amputee himself as a result of enemy wounds received in Korea.

PUBLIC HEALTH SERVICE

Warning Against Psittacosis.—Dr. Leonard A. Scheele, Surgeon General, warned physicians and the public Feb. 27 to be on the alert for psittacosis, a virus disease which produces symptoms similar to those of influenza and pneumonia. It may be treated with antibiotic drugs. Dr. A. J. Chesley, Minnesota State Health Officer, has determined that two human cases of psittacosis in his state were contracted from a parakeet transported from southern Florida. Dr. Scheele cautioned that additional cases may be occurring in many parts of the United States, as islets are known to have purchased and transported tropical birds from the infected area. He emphasized that, although there is no real danger of a widespread epidemic, both physicians and the public should be on the alert for the possibility of illness traceable to psittacine birds brought in from the affected area.

Specialists from the Public Health Service's Communicable Disease Center at Atlanta, Ga., are assisting the Florida State Board of Health in tracking down sources of psittacosis infection at bird farms and stores in the state.

Changes made in the Interstate Quarantine Regulations, effective last November, remove all federal restrictions on shipments of psittacine birds from psittacosis-free areas in the United States. However, they also prohibit the shipment of birds from areas where the Surgeon General has determined that psittacosis infection is dangerous to the public health. To date there have been no cases of parrot fever diagnosed in humans in Florida, but Public Health Service and private physicians are on the lookout for possible victims.

Dr. Scheele urged physicians to report promptly all human cases, as well as cases of illness among birds, to public health authorities so that investigations can be made to determine the origin of the infections and to institute appropriate control measures. Psittacosis is spread by many types of birds, but infected parakeets, parrots, and related birds of the psittacine family are principally responsible. The psittacine group includes, besides parrots and parakeets, Amazons, Mexican double heads, African grays, cockatoos, lovebirds, lorries, and lorikeets. Because of their immediate contact with these birds as household pets, owners and handlers are in the most danger from parrot fever.

New Head of Communicable Disease Center.—Dr. Vernon B. Link has been designated deputy officer in charge of the Communicable Disease Center, Atlanta, succeeding Dr. Andrews, who was deputy officer in charge for six years. Dr. Link, an authority on plague and other rodent-borne diseases, was transferred to the headquarters of the Communicable Disease Center from San Francisco, where for more than a year he was head of the center's plague investigations section. Dr. Link was commissioned in the Public Health Service in 1936. In 1946-47 he headed the epidemiology division of the Communicable Disease Center and its predecessor organization.

Public Health Aid for Formosa and the Philippines.—Two Public Health Service officers, Emily Myrtle Smith and Genevieve Soller, are the first nurses assigned to Formosa and the Philippine Islands under the Mutual Security Agency program, the Federal Security Agency announces. Miss Smith will be stationed in Taipei and Mrs. Soller in Manila. They will be chief nurse consultants to the MSA missions in the two capitals. They will work with nurses and other health workers to develop schools of nursing and to extend public health nursing in the two countries, particularly in the rural areas.

In addition to public health, MSA is providing technical and material assistance to improve other essential public services in Formosa and the Philippines and to aid in the development of their agricultural and industrial production.

Laboratory Diagnosis of Rabies.—A short course in the laboratory diagnosis of rabies will be given at the Laboratories of the Communicable Disease Center in Chamblee, Ga., April 7-11. The course will be of a refresher-type in laboratory training in the various aspects of rabies diagnosis. The instructors will be members of the staff of the Communicable Disease Center, guest lecturers, and consultants. There will be no tuition or laboratory fees, but travel and living expenses must be paid by the technician or his employer. Applications should be addressed to Dr. R. F. Reider, Laboratory Training Services, Communicable Disease Center, P. O. Box 185, Chamblee, Ga.

VETERANS ADMINISTRATION

Neurosurgical Residency.—A neurosurgical residency will be available at Cushing Veterans Administration Hospital, Framingham, Mass., on July 1. This program has two-year approval by the American Board of Neurologic Surgery. Fulfillment of board requirements is assured through direct affiliation with the Lahey Clinic and the Graduate Hospital of the University of Pennsylvania. One year of general surgical training may be arranged if necessary. The residency is under the supervision of the deans' committee in the Boston area. Salary begins at \$2,400 per year.

New Hospital Managers.—Dr. Albert H. Fechner has been appointed manager of the 546 bed neuropsychiatric hospital in Salt Lake City, which is scheduled for completion in April, 1952, and Dr. Benjamin A. Cockrell, has been appointed manager of the 300 bed tuberculosis hospital in Memphis to succeed Dr. Glen W. Doolen, who is transferring to the central office in Washington, D. C. Dr. Fechner is now chief of the hospital psychiatry section of the psychiatry and neurology division in the central office. He first became associated with the VA in June, 1947, as chief of neuropsychiatry in the former VA branch office at Denver. Dr. Cockrell is now the chief medical officer of the VA Regional Office at Chicago.

Hospital News.—Dr. Lothar B. Kalinowsky of the New York Psychiatric Institute recently addressed the staff at the Veterans Administration Hospital, Northport, Long Island, N. Y., on the indications and limitations of prefrontal lobotomy.

FOREIGN LETTERS

BRAZIL

Blood Donors and Brucellosis.—The presence of positive reactors to brucellosis among blood donors was observed formerly by Brito Mena in Mexico. In Brazil, among 833 blood donor candidates examined by Dr. Genésio Pacheco, the Brucella agglutination test showed an incidence approximately equal to that found among 385 hospital patients. Of the 1,218 serums examined in these two groups, 5.23% gave positive results. When dealing with apparently healthy persons, the general index obtained was 4 per 100,000, approximately the figure obtained in other countries. Considering that apparently healthy patients may have Brucella in the circulating blood, the elimination of positive Brucella reactors is necessary in the selection of blood donors, particularly since these patients are in precarious conditions of physical resistance and are prone to infection with small numbers of bacteria.

Burns of the Hand.—The treatment of the burned hand requires great care from the moment of the accident until complete recovery is obtained. The patient should be under constant and careful medical care, in order to preserve all the structures that have not been destroyed by heat and to prevent, minimize, and cure the resulting deformities, as pointed out by Dr. Victor Spina of São Paulo, who manages such cases frequently.

In burns of the hands Dr. Spina generally removes the foreign bodies and makes an occlusive and compressive dressing, wrapping each finger separately. He does not open the blebs. The limb is elevated in order to minimize edema, and the hand is kept in functional position. He prescribes intramuscular penicillin and oral sulfadiazine. The dressing is removed after 8 to 10 days, and at this moment functional reactivation may be started. The patient will be encouraged to make active movements of all joints with the hand submerged in normal saline solution.

All first degree burns heal spontaneously, generally after two or three weeks. Deeper burns require skin transplants in order to epithelize. Epithelization must be obtained as soon as possible, in order to permit functional reeducation before important alterations occur in the deep structures. The chief objective is preservation of function. In these cases Dr. Spina prefers the use of small thin grafts, which promote rapid epithelization of the burned area and which permit earlier institution of physiotherapy.

When the burn is deep and bones, tendons, and joints are exposed, it is necessary to use pedicle grafts for two reasons: (1) because free grafts have no power of integration on these elements; and (2) because the utilization of a pedicle flap represents an indispensable condition for a probable later operation on joints, tendons, and bones.

In spite of proper treatment, severe burns of the hand may produce deformities. The sequels of burns of the hands present great polymorphism, and some offer no possibility of functional recuperation. Depending on the localization of the burn, the palmar or dorsal surface of the hand may be the site of sequels, which may or may not be followed by interdigital synchias.

The plan of treatment, surgical or associated with physiotherapeutic measures, depends on the extent of injury of the different elements responsible for the dynamics of the hand. Therefore, the exact diagnosis of the lesion is of exceptional importance. When the retraction is due only to the cutaneous scar, treatment consists in the excision of all the scar and immediate placement of an intermediate skin graft; the hand must be immobilized in hypercorrection in a plaster cast, in hyperflexion in the contractures of the dorsal side, and in hyperextension in contractures of the palmar side. Physiokineto-

therapy is of great value as a complement to the surgical treatment. When there is also injury to joints, tendons, and bones, the cutaneous scar is covered by a pedicle flap, because it may be necessary to operate on these parts afterwards. To correct deformities of the hand physiotherapy is indispensable. According to Dr. Spina, the specialist must know the technique and exact moment when the treatment is to be started. When physiotherapy is well done it may completely cure the patient, but if it is done by unskilled persons it may aggravate the condition.

DENMARK

Danish Tuberculosis Index.—At the end of 1951, the three-year tuberculosis survey of Denmark was successfully completed. It included mass radiography of different age groups and yielded invaluable information that will form the basis of a large central card index system known as the Danish Tuberculosis Index. This system, the outcome of cooperation of the Danish Ministry of Health and the tuberculosis centers in Denmark with the World Health Organization, will centralize the findings of the recent survey. The survey revealed that about one new case of open tuberculosis was found in every 2,000 persons examined. This comparatively low rate reflects the efficiency with which tuberculosis work has been carried out in Denmark in the past. It must, however, be admitted that the search for cases of tuberculosis has not been uniformly successful in the older age group, in which patients with open tuberculosis are likely to shun mass radiography. This may be one of the reasons why some 3,000 new cases of tuberculosis are still being discovered every year in Denmark, with its population of only 4,000,000.

A main object of the Danish tuberculosis survey was to promote BCG vaccination of the tuberculin-negative section of the population. Almost all tuberculin-negative persons gladly accepted this vaccination, but hitherto, the recording of BCG vaccinations has not been sufficiently systematic. For several years, the State Serum Institute in Copenhagen has urged physicians to send in reports on the number of vaccinations and the tuberculin reactions before and after vaccination, but the response has not been completely satisfactory. The Danish Ministry of Health recently circularized the medical profession on this matter. Physicians were requested to report all vaccinations that they had done, both primary vaccinations and revaccinations, to the State Serum Institute. It is hoped that the data thus provided will, in a few years, yield useful information. Tuberculin allergy may not always be a true index of immunity to tuberculosis. To gauge the effects of the BCG vaccination, it is necessary to secure reliable statistics regarding tuberculosis morbidity and mortality in the community, in relation to the number of persons who have been vaccinated with BCG.

Too Many Blood Transfusions?—At the Surgical Department of the Rigshospital, in Copenhagen, Dr. Ove Noring and Dr. Knud-Erik Sjölin have endeavored to determine whether there is complete justification for the system, adopted in certain hospitals, of making blood transfusion for major operations a matter of almost wholesale routine. They have made increasing use of this measure in their hospital in recent years, but they have by no means adopted it as a routine measure independent of the needs of each patient. They wondered if this discrimination had unfortunate consequence in the cases ending fatally. The material on which they base their investigations consists of the 345 patients, who, during the period 1946 to 1949, suffered from chronic gastric ulcer for which they were operated on under lumbar anesthesia, supplemented, in some cases, by inhalation anesthesia. Blood transfusion was given before the operation to three patients, because of severe anemia. It was given to 43 patients (12.5%) after the operation; the indication for this

measure was shock or incipient shock in 21 of the patients. There were 17 deaths among the 345 patients, and, in 5 patients with fatal cases, no blood transfusion was given. The death of one patient was caused by pulmonary embolism, the death of another by pulmonary edema caused by disease of the myocardium, and in three patients, infections of the lungs had fatal results. A scrutiny of these five fatalities led to the conclusion that death could probably not have been prevented by blood transfusion. The authors of this study, which is published in *Nordisk Medicine* Dec. 12, 1951, quoted the following statement found in a recent editorial in the *British Medical Journal*: "Now that it is so easy to obtain blood and plasma, they tend to be transfused too readily. No transfusion should be given until the medical man in charge of a case is convinced that it is really necessary, and even then the risks must be borne in mind."

Operative Treatment of Congenital Pyloric Stenosis.—In 1948, Winkel Smith published a study covering five hospitals in Copenhagen over a 10 year period and dealing with 531 patients with congenital stenosis of the pylorus who were given medical treatment. There were 17 deaths in this series, whereas there were no deaths among the 15 patients given operative treatment. This comparatively high mortality rate among medically treated patients depended, to a considerable extent, on the prolonged stay in hospital and the consequent risk of hospital infection. The average stay in the hospital of the 531 medically treated patients was 74 days.

Since 1947, almost every patient with stenosis of the pylorus admitted to the Children's Department of the Rigshospital (to which Dr. Winkel Smith is attached as a consultant surgeon) has been given operative treatment. Between 1947 and 1950, a total of 94 such patients were operated on. The results were analyzed by Dr. Jørgen Vesterdal, who has added eight similar cases from another hospital to his report, bringing the total to 102 patients (90 boys and 12 girls). In 41 of these patients attempts were made to effect a cure by medical treatment at home or in a hospital. The Fredet-Ramstedt operation, recently described by Ladd and Cross, was performed. There were no deaths in the hospital, and the patients were discharged after about 15 days. A follow-up study from four months to four years after the operation showed that there had been only two deaths; neither was caused by the operation. All 84 patients had been well after discharge; and 11 babies had thrived, in spite of slight vomiting. In the remaining five patients, there were disturbances such as dyspepsia.

In discussing the comparative merits of medical and operative treatment, Dr. Vesterdal points out that the prospects of successful operative treatment can be enhanced by prompt operative intervention before valuable time has been lost and the patient has been debilitated by prolonged ineffective medical treatment. Accurate figures are not forthcoming with regard to the frequency of the occurrence of congenital stenosis of the pylorus, in Denmark. But in Sweden, Wallgren has calculated that there is one such case for every 150 boys and for every 775 girls.

Physicians' Waiting Rooms Under Fire.—Severe criticism of physicians' waiting rooms has lately been voiced in the Norwegian lay press and the Danish medical press. A layman writing in a lay Norwegian daily expressed peevish discontent with typical physicians' waiting rooms in which patients are confronted by uncomfortable wooden chairs, lugubrious fellow patients, and, worst of all, wretched reading matter. Why, this complainant wails, should barbers equip their shops with the latest editions of the daily press and illustrated journals of high artistic standard and appeal while doctors think any rubbish good enough for their patients, who, they suspect, purloin any reading matter that is attractive.

In the Danish medical press, the attack on physicians' waiting rooms is written from the bacteriological rather than the sociologic angle. The suggestion that the bacterial flora of the literature of these waiting rooms grows with the staleness of the printed pages has been challenged. An attempt was made to determine whether a human being has ever been infected by printed matter in a physician's waiting room. This question recalled an important work that was published in 1938 by Dr. Walbum, whose investigations were undertaken at the request

of the Danish State Library Service. He studied the behavior of staphylococci in books of various ages and subjected to various temperatures. He found that by gradual heating up to a temperature of about 60 C for 24 hours, books could be disinfected both outside and inside, without being damaged. He also drew attention to the disinfectant action of printers' ink. This discussion has led one contributor to suggest that the hygiene of physicians' waiting rooms would prove an attractive subject for a doctoral thesis.

GERMANY

Annual Meeting of the German Medical Association.—The *Deutscher Aertzetag*, the association of physicians' groups in the Federal Republic of Western Germany, held its annual meeting on Oct. 4, 1951, at Munich. Comprising the Aerztetage are the Aerztetage, which are semiofficial medical organizations on the state level, in which membership in most cases is compulsory; the Kassenaerztliche Vereinigung, made up of physicians on the panels of compulsory health insurance; the Marburger Bund, an association of hospital resident physicians; the Verband der Chefaerzte, the organization of medical directors of hospitals; the Verband der Aerzte des oeffentlichen Gesundheitsdienstes, the association of public health officers; and the Verband der Aerzte Deutschlands, which protects the economic interests of physicians.

The main topic of the meeting was preventive medicine. Three papers dealing with public health problems were read at the opening meeting. Prof. Karl Coerper, secretary of the Arbeitsgemeinschaft fuer Gesundheitswesen (Working Association for Public Health) spoke on the development of a system of health protection and preventive medical service. Dr. Coerper proposed the establishment of a system of family examinations, based on regular yearly physical examinations and combined with investigation into each family's social background. A special publicly financed service would be established, consisting of physicians specially trained in preventive medicine who would constitute a link between the practicing physicians and the health departments. Of greatest importance, however, was the stress that was laid on the prevention of illness through early diagnosis of heart disease, cancer, rheumatic illnesses, and communicable diseases. Indirectly, the idea of positive health was the main theme of this paper.

Dr. Ernst Fromm, chief of clinical laboratories of the city hospital at Harburg, emphasized the deplorable situation existing in the German hospital system. Due to inadequate physical facilities and the economic plight of the medical and nursing staffs, German hospitals cannot meet modern requirements of medical care. The hospital administration is in the hands of lay persons who have no special training and whose main interest is the balancing of the hospital budget, regardless of medical needs. The medical director is pushed into the background and cannot exert any appreciable influence on the administration.

Dr. Walter Landauer, of the Kassenaerztliche Vereinigungen (organizations of insurance panel physicians) spoke on prevention and treatment of illness. He emphasized the importance of promoting preventive medicine in order to ease the tremendous load that, at the present time, is carried by the practicing physicians, the hospitals, and the health insurance system. Dr. Landauer pointed out the inter-relationship between preventive medicine and curative medicine. He declared that the savings effected by preventive medical measures in the use of medical facilities, in the saving of productive life, and in the prevention of early disability would far outweigh the expenses incurred in a generous public health program.

During the discussion much criticism was voiced against certain aspects of the preventive medical program as developed by the speakers; however, the idea was generally accepted that preventive medicine should play a role in the physicians' work equal to that of curative medicine. The existing system of social insurance was severely criticized by some speakers and blamed for many of the difficulties that now stand in the way of adequate medical care.

ITALY

National Convention of Surgery.—The 53rd National Convention of the Italian Society of Surgeons was held in Rome and attended by many specialists and surgeons from the University clinics of Italy. Prof. Raffaele Paolucci, Director, Surgical Clinic, University of Rome, delivered the inaugural address, in which he emphasized the recent achievements of surgery. For the first time in Italy, surgical operations were televised between sessions.

Resuscitation in Surgery.—Prof. A. M. Dogliotti and Professor Costantini, from the Clinic of Turin, presented a paper, which disclosed that the possibilities of acute and severe incidents that may occur during or after surgery and that may endanger the patient's life have increased simultaneously with increasing indications for operations. Means for preventing and for combating the occurrence of these complications are being improved, and today it is possible to resuscitate patients that some years ago would have been considered lost. Of the incidents endangering the patient's life, acute anemia secondary to hemorrhage and associated with phenomena of collapse is of great interest. The usual methods of treating collapse due to hemorrhage are transfusions of blood, plasma, or its substitutes. The speakers particularly studied intra-arterial transfusions. This may save patients in whom intravenous transfusion may be inefficient and sometimes even harmful, because it may cause an excessive load on the venous system and on the right side of the heart. But in some patients, because of the initial vascular collapse or because of the time that has elapsed since the hemorrhage, even transfusion into the arteries may fail. According to the speakers, some of these patients may still survive if transfusion into the carotid artery in a cranial direction is attempted.

The speakers tested this technique in animals, the experiments being based on the assumption that in collapse due to hemorrhage the most urgent thing is to restore the blood flow in the higher centers. The method proved very efficient, inducing resuscitation even a few minutes after the blood flow had completely stopped. After numerous experiments indicated its usefulness and harmlessness, it was tried successfully in man. The method gave results comparable to, or even greater than, those obtained with direct massage of the heart although simpler and less dangerous maneuvers are used.

Varices of Lower Extremities.—Professor Torraca, Director, Surgical Clinic, University of Naples, presented a paper on indications for, and results of, surgical treatment of varices of the legs. Prof. Rodinó, from the University of Naples, reported on anatomic data concerning the venous systems of the leg and discussed briefly the physiology of the venous circulation of this part of the body. In the diagnostic study of varices of the leg a limitation to a generic diagnosis is today impossible because other points of fundamental importance must be defined, i. e., (1) whether it is a secondary varix, mainly with intra-abdominal compression; (2) whether valvular insufficiency of the saphenous veins is present; (3) whether insufficiency of the communicating veins is present; and (4) whether the deep circulation is pervious. Intraosseal phlebography is useful for exploration of the deep circulation especially in cases of "postphlebotic leg." With regard to treatment, the speaker mentioned the inconveniences that may arise from sclerosing therapy, one of which is the possibility of recurrence and danger of embolism. To avoid these inconveniences sclerosing therapy has been combined with preventive ligation of the saphenous vein and this method is today accepted by all modern surgeons. At the clinic of Naples, preference is given to high ligation of the saphenous vein and ligation of all the collateral vessels combined with saphenectomy in the thigh. Recurrence and partial success of the surgical treatment are attributable to insufficient technique and mainly to the fact that anatomic anomalies were not detected.

Obstructions of the Hepatic and Common Bile Ducts.—Hepatic and common bile duct obstruction was discussed in cooperation with the Society of Internal Medicine, which was also holding its national convention. Professor Ceccarelli, director of the clinic of Padua, who reported on the surgical aspects of the subject, pointed out the three types of operations that may be performed in cases of obstructions of the hepatic

and common bile ducts, i. e., (1) removal of the obstruction that interferes with the flow, like calculi, parasites, and intrinsic tumors, (2) restoration of the continuity of the biliary tree as in instances of restrictions and stenosis, (3) formation of a new way of discharge into or, in exceptional cases, outside of the digestive tract. Considering the therapeutic methods indicated for each obstructive cause, the speaker emphasized the importance of roentgen manometric studies during operation in instances of functional obstructions. Of great interest are cicatricial contractions of the biliary tract that may be spontaneous or, mainly, postoperative. In these instances restoration of the biliary outflow into the digestive tract may be obtained either with plastics or anastomoses aiming to reconstruct the main biliary passage or with operative formation of an anastomosis between the bile duct and the digestive tract. Systematic practice of cholangiography during operation evidenced the high incidence of lithiasis of the gallbladder and the common bile duct. Tumors of the hepatic duct constitute a very small percentage of the diseases of the biliary passages. Obstructions extrinsic to the hepatic duct may be benign or malignant. The latter forms are due to carcinoma of the head of the pancreas.

LONDON

Amending the Health Service Act.—The British Medical Association council has issued its first interim report on the reform of the National Health Service Act. The council sat for eight hours on Sept. 26, 1951, and discussed the recommendations of its amending acts committee.

The report contained 26 recommendations and two long appendices. Most of the recommendations were accepted as they stood, some were amended, and one or two withdrawn or referred back to the committee. By this work, the British Medical Association is building an outline for use in future legislation that they think will make a reformed national health service of greater benefit to the population and more satisfactory to the profession. One section of the report deals with powers of the Minister of Health. Article 26 states that one of the most striking and dangerous features of the National Health Service Act is the wide power given to the minister to make regulations and to prescribe by order. Of the 79 clauses and 10 schedules in the act for England and Wales, no fewer than 44 confer on the minister power to make regulations or orders. In general, all regulations are subject to parliamentary control, but, unless there is provision to the contrary, orders are not subject to such control. It is recommended that, with reference to section 5 of the National Health Act of 1946, maximum charges should be laid down only in consultation and agreement with representatives of the profession, that the power of the minister to acquire privately owned equipment, compulsorily, and to pay for it at a rate to be decided by the treasury should be repealed, and that the National Health Service Act, 1949, should be amended so as to limit the minister's power and to require him either to accept such schemes as are submitted by a local authority or to refer them back for reconsideration. They also recommend that the power of the ministry to prescribe the terms of service of family physicians by regulation and to make provision for the issue of an unlimited number of certificates without payment should be repealed and replaced by the procedure recommended by the council. For instance, the minister's power to change the regulations in respect of remuneration or conditions of service of any sections of the profession should be restricted to those conditions that are either agreed on by the medical profession or determined by arbitration.

In dealing with the question of private beds in hospitals, the committee recommends that adequate pay-bed accommodations should be set aside in all hospitals where a need can be shown to exist. The charges for a private bed should be reduced to a reasonable level, and the right of a patient to receive free hospital accommodations, under the act, should be recognized by allowing him, in effect, a grant-in-aid toward accommodation in a private bed. The committee further recommends that, as far as possible, charges for private beds should be standardized in each group of hospitals.

The report makes many recommendations designed, in the light of experience, to modify the National Health Act, to eliminate red tape, to give better service to patients, and to free the physicians, as much as possible, from frustration and from the innumerable clerical duties that seem part of the work of every government servant.

A general meeting of the St. Marylebone division of the British Medical Association, which numbers nearly 1,000 consultants amongst its members, was held under the chairmanship of Dr. Lawrence Abel, a surgeon, on Nov. 19.

It was decided to support the recommendation of the council of the British Medical Association that there should be established a special national health service court of arbitration for settling disputes between the profession and the government. It was also decided to support various recommendations aimed at limiting the minister's power. The meeting favored a larger representation of duly elected medical members to serve on regional hospital boards. The members also decided to press for the right of all patients, whether public or private, to obtain their drugs and appliances at public expense.

At the same meeting, a discussion took place on the subject of the establishment of a college of general practice. In opening the discussion, Dr. John H. Hunt, of London, who is a private medical practitioner, pointed out that the specialist branches of the profession have their own colleges but that there is no headquarters for general practitioners. He felt an active and influential college would greatly help the family physicians in academic and educational affairs and provide the leadership that is now so sadly lacking. Such a college would be nonpolitical, and he acknowledged the help he had received from the Academy of General Practice of the U. S. Coordinating committees would be set up to implement new ideas for the furtherance of family physicians' interests. Lectures and discussions would be arranged to foster postgraduate more than undergraduate teaching. Exchange visits to overseas would be arranged and any "brain-waves" by family physicians would be published. Such a college, he maintained, would foster the ethical traditions of medical practice and form a center at which members and ideals could rally. Facilities would be arranged so that family physicians could undertake research, and he felt that such a college would improve the status and prestige of practitioners and improve the quality of their practice. The time might come when a higher examination or even a diploma in "general practice" would become available. In general terms, the members of the meeting expressed sympathy with the idea and promised all possible practical help.

National Anti-Influenzal Measures.—Large scale national plans to combat an epidemic of influenza have been announced in the *Monthly Bulletin of the Ministry of Health*. Medical officers of health are requested to make arrangements with selected general practitioners in their areas, who will act as "spotters" and furnish regular reports on the incidence of influenza in their practices, especially when there is a sudden increase in attendance at their offices or in requests for domiciliary visits. Arrangements are also to be made for medical officers at industrial concerns, residential communities, such as boarding schools, and units of the armed services to notify medical officers of health when there is a significant increase in absenteeism due to upper respiratory disease in the industry or community. Medical officers at seaports and airports are requested to report promptly the occurrence of influenza-like illnesses among incoming passengers or crews. Arrangements have also been made for the Ministry of National Insurance to notify medical officers of health immediately when the number of sickness benefit claims shows a sharp rise. The registrar-general has allowed registrars to supply medical officers of health with daily reports on total deaths and deaths from pneumonia, bronchitis, and influenza during an epidemic. On the basis of this information, medical officers of health will notify hospitals in their areas of an impending attack, so that arrangements can be made for freeing beds for the admission of selected cases. In addition to the beneficial effect this will have in allowing severe cases to be admitted to a hospital immediately, it will provide an opportunity for an investigation of the effect of new remedies in these cases. Plans are to be

made forthwith by medical officers of health and directors of public health laboratories to isolate samples of virus at the beginning of an epidemic. This will not only allow the isolation of representative strains but will also help to differentiate influenza from other forms of upper respiratory infection. Finally, "the Ministry of Health has decided to support the production of influenza virus egg vaccine and the Medical Research Council will soon announce the appointment of a committee to study the technique of vaccine production and administration and to promote extensive field trials." The *Times* has remarked, "never before has an attack on influenza by vaccines received so much official encouragement."

MEXICO

Fourth Pan American Congress of Ophthalmology.—In 1939, the Pan American Association of Ophthalmology decided to hold a Pan American Congress every four years. The Fourth Congress, which took place from Jan. 6 to 12, 1952, at Mexico City, was attended by more than 800 ophthalmologists from 18 North, Central, and South American countries and from France, Spain, England, and Germany. Among the official delegates were Dr. Conrad Berens, U. S. A., president of the Pan-American Association of Ophthalmology; Dr. Edmond Velter, France; Dr. Hermenegildo Arruga, Spain; Dr. Rudolph Thiel, Germany; Dr. René Contardo, Chile; Dr. Alberto Urrets and Dr. Gunter von Grohman, Argentina; Sir Stewart Duke-Elder, England; Dr. Bernard Samuels, Dr. Peter Kronfeld, Dr. Algernon B. Reese, and Dr. Ludwig von Sallman, U. S. A.; and Dr. Antonio Torres Estrada, Dr. Magin Puig Solanes, and Dr. Luis Sánchez Buñes, Mexico.

The scientific activities of the congress included official addresses, the reading of more than 150 papers, and symposia, the most important of which were recent advances in American tropical ophthalmology, virus and ophthalmology, ophthalmology in aviation, the role of cysticercosis in ocular pathology, recent advances regarding primitive glaucoma, pediatric ophthalmology, the role of heredity in ophthalmology, and recent advances in ophthalmologic therapeutics. All important communications were translated from Spanish into English or vice versa.

SPAIN

Tribute to Jaime Ferrán y Clua.—A few years ago, the Society of Physicians of Barcelona invited the Spanish medical profession to request from the government the organization of a national tribute to the memory of Dr. Jaime Ferrán y Clua, the developer of cholera vaccine, in 1952, the centennial of his birth. On May 15, 1949, the ministry of state ordered a national festival in memory of Dr. Ferrán, to be sponsored by the government. The ministry of state nominated the Consejo General de Colegios Médicos (Spanish Medical Association) to represent the medical profession of Spain in opening an account in the Banco de España and in managing this sum of money, which he called "Account for Homage to Dr. Ferrán." It will include all donations given for this purpose by official organizations and individual persons. Hospitals and professional, cultural, and other scientific centers will contribute. The ministry of state gave 25,000 pesetas as the first donation to the fund.

The Ministry of National Education recently organized the Instituto Bacteriológico Jaime Ferrán, as a dependency of the National Council of Scientific Research. Dr. Socias Amoros has been appointed technical director of the institute. The ministry of state will print a Ferrán mail stamp. Busts of Ferrán will be unveiled by the municipal authorities of Barcelona, Tarragona, and Madrid. The fountain in the street de la Princesa, near the headquarters of the General Department of Public Health, will be dedicated to the memory of Ferrán. Literary sessions will be held, and a Ferrán annual award for bacteriologists either in Spain or in foreign countries will be established.

BUREAU OF LEGAL MEDICINE AND LEGISLATION

MEDICOLEGAL ABSTRACTS

Admissibility in Evidence of Chemical Tests for Intoxication.—The defendant was charged with driving a motor vehicle while under the influence of intoxicating liquor and was found guilty by a court hearing the case without a jury. From this finding of guilty, and the judgment which was entered thereon, the defendant appealed to the appellate court of Illinois.

At about 5 o'clock one afternoon the defendant was involved in an automobile collision in the city of Chicago, and at 6:45 p. m. the same day was taken to the Chicago Police Scientific Crime Detection laboratory where he voluntarily submitted to a test on the Harger Drunkometer, a device used to test the alcoholic content of a subject's breath. Daniel T. Dragel, evidence evaluator at the Crime Detection Laboratory, who operated the Drunkometer, testified that the test applied to the defendant disclosed that he had a concentration of alcohol in the blood of 0.30%, and that in his opinion the defendant was under the influence of alcohol at the time of his arrest. The police officers who arrested the defendant gave similar opinions. The defendant, on the other hand, testified that before the collision he drank two glasses of beer and that he had not consumed any other alcoholic beverages during that day. He contended that the trial court erred in permitting the introduction in evidence of testimony concerning the Drunkometer test and the result shown thereby, on the grounds that the Drunkometer had not received general scientific recognition as an accurate index of the amount of alcohol in the blood.

The underlying theory and operation of the Drunkometer was explained in great detail by the State's witnesses, Dr. R. N. Harger, the inventor, Dr. Clarence Muehlberger, and Dragel, a graduate chemist and employee of the City Police Department for fifteen years. In making the test it appears that the subject inflates a small balloon. The exhaled breath of the subject trapped in the balloon is then allowed to pass through a reaction chamber which contains measured amounts of potassium permanganate and sulphuric acid. When a certain amount of alcohol passes through the solution it causes a change in the color of the chemicals. The concentration of alcohol in the breath can be computed from the amount of breath required to cause the chemical reaction, and from this the alcoholic content of the subject's blood. There is 2,000 times as much alcohol in a given amount of blood as there is in a like amount of the breath of the same subject. Mr. Dragel testified, among other things, that the Drunkometer test applied to the defendant indicated the accumulation in his body of alcohol equivalent to that of about 10 oz. of 100-proof whiskey or ten full bottles of beer. Dr. Harger, Professor of Biochemistry and Toxicology at the Indiana University School of Medicine, testified that for several years he had been consultant on poisons for the Indiana State Board of Health; that for the past 25 years he has conducted research on toxicology and alcohol; that in approximately one thousand tests he has taken blood and breath of the subject at the same time; that he has conducted thousands of breath tests and he found that by means of the breath method he can accurately predict the percentage of alcohol in the blood and that all persons would be under the influence of alcohol when the alcoholic blood content is above 0.15%. Dr. Muehlberger, a toxicologist, employed by the Michigan Department of Health Laboratory for the past eight years, testified that from 1930 to 1941 he was a coroner's toxicologist in Cook County; that during this period he was a professor of Toxicology in Northwestern University, University of Illinois College of Medicine, and University of Chicago Medical School; that since 1923 he has made innumerable tests of breath, blood, urine, saliva, and organs, to determine their alcoholic content; that alcohol is absorbed from the gastrointestinal tract into the bloodstream which distributes

it to all parts of the body; that alcohol thus distributed has a numbing effect on the nerves of the body and that there is a progressive deterioration of nerve function which causes varying degrees of intoxication; that alcohol which enters the lung is excreted in the breath; that the concentration of alcohol in the breathed air is about one two-thousandth of the concentration of alcohol in the blood; that all persons having alcohol blood content above 0.15% are under the influence of alcohol; and that the amount of alcohol in the blood of a subject may be reliably and accurately determined by the amount of alcohol in the breath, by means of the Harger Drunkometer.

The defendant relied on a Michigan case, *People v. Morse*, 325 Michigan, 270 (38 N. W. (2d) 322, Mich. 1949) (*J. A. M. A.* 141:740 [Nov. 5] 1949), an appeal from a conviction of negligent homicide, in which the admission into evidence of testimony concerning the Harger Drunkometer and the results of the test was held to be reversible error. In that case there was testimony for the State by two policemen, both trained in chemistry, one of whom studied the Drunkometer for one month under the direction of Dr. Harger and then instructed the other, and by a doctor who had worked as a student assistant to Dr. Harger. Five doctors called by the defense testified in substance that most of the medical profession did not consider the device reliable. In a more recent case (*McKay v. State*, 235 S. W. (2d) 173, (Texas, 1951) (*J. A. M. A.* 146:867 [June 30] 1951), said the court, the defendant was charged with the same offense and raised the same objections as in the case at bar. There the court held that evidence of the result of the Harger Drunkometer test was admissible. The question here presented, the court continued, has never been ruled on by the courts of review in Illinois.

Medical science recognizes 60 pathological conditions which produce symptoms similar to those produced by alcohol yet the law permits nonexpert, lay witnesses to testify to objective symptoms commonly associated with alcoholic intoxication on the theory that sobriety or intoxication are matters of common knowledge. The defendant argued that there is a lack of unanimity in the medical profession as to whether intoxication can be determined by breath. Even so, we think this objection goes to the weight of the testimony and does not destroy its admissibility. The evidence in this case shows that the experts called by the state are eminently qualified in the field in question. We think, the court concluded, that the evidence is sufficient to warrant a finding by the trial court that the defendant was under the influence of intoxicating liquor, so that his driving ability was impaired within the meaning of the statute, without evidence of the drunkometer test. Since we hold that evidence of the breath test is admissible, the state is not compelled to rely solely on the opinions of nonexpert witnesses to prove the offense charged. Accordingly, the judgment of conviction was sustained.—*People v. Bobczyk*, 99 N. E. (2d) 567 (Illinois 1951).

MEDICAL MOTION PICTURES

Wonderland of Vision: 16 mm., color, sound, showing time 21 minutes. Produced in 1950 by Proser-Barnes Productions, New York for and procurable on loan or purchase from the Better Vision Institute, Inc., 630 Fifth Avenue, New York 20.

This motion picture begins by briefly explaining the different parts of the eye, how they work together, and how lenses focus light rays. The greater part of the film shows and explains the steps in the manufacture of optical glass, the fabrication of frames, and the finishing of lenses. It concludes with a fashion sequence showing models wearing glasses. The film is not intended to nor does it deal with diseases of the eye. It is concerned only with refraction as measured by optical methods. The entire film is interesting and informative and is enhanced by good narration, photography, color, and choice of material. It would be of interest to most lay audiences and might be of value to the physician lecturing to the laity on this general subject.

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Am. Journal Diseases Child., Chicago

82:519-654 (Nov.) 1951

- Nonendocrine Deviations from Normal Pattern of Osseous Development. R. Wagner.—p. 519.
- Physical Changes Associated with Adolescence in Boys. E. L. Reynolds and J. V. Wines.—p. 529.
- *Use of Desoxycorticosterone Acetate in Dehydration and Malnutrition in Infancy. J. A. Bigler and H. S. Traisman.—p. 548.
- Blood Level of Thiamine in Normal Children. H. A. Waisman, Tong Soo Cho, J. B. Richmond and S. J. Williams.—p. 555.
- Arteriosclerosis in Infancy. B. L. Lipman, I. M. Rosenthal and H. Lowenburg Jr.—p. 561.
- Salmonella Meningitis: Recovery from Meningitis Due to Salmonella Sp. (Type Montevideo), with Consideration of Problem of Salmonella Meningitis. M. L. Beene, A. E. Hansen and M. Fulton.—p. 567.
- Neurofibromatosis in a Newborn Infant. B. E. Scott and H. J. Cohen.—p. 574.
- Endocardial Fibroelastosis. W. T. Hill and W. A. Reilly.—p. 579.
- Adenoma of Bronchus in a Nine-Year-Old Child. S. Smoller and A. De L. Maynard.—p. 587.
- Causes of Congenital Defects: Review. F. C. Fraser and T. D. Fainstat.—p. 593.

Desoxycorticosterone in Infants with Malnutrition.—The 10 infants reported in this paper were from 3½ weeks to 12 months of age, all but one being less than 6 months old. They cannot be considered to have had proved adrenal cortical deficiency, but they did have some symptoms of such deficiency, particularly dehydration and malnutrition. Two presented some clinical evidence of adrenal cortical hypofunction as the cause of disturbances of mineral metabolism. Therapeutic response to desoxycorticosterone acetate and salt was dramatic in all but one patient, who was markedly dehydrated after colostomy for agenesis of the myenteric plexus and did not respond to any treatment. Most of the infants received 2.5 mg. of desoxycorticosterone acetate and 1 gm. of sodium chloride daily for as long as 17 days, but the majority were treated less than 8 days. The clinical results suggest that desoxycorticosterone acetate and sodium chloride deserve further trial in treatment of malnourished and dehydrated infants who have not responded to standard management. This is purely an empirical method of treatment. The exact role of the adrenal gland in the condition of these patients is not known. Patients receiving desoxycorticosterone acetate should be watched carefully for the development of edema.

82:655-788 (Dec.) 1951

- Specific Treatment of Children with Tuberculosis. E. M. Lincoln and V. N. Wilking.—p. 655.
- *Allergic Dermal-Respiratory Syndrome in Children. B. Ratner, C. Collins-Williams and S. Untracht.—p. 666.
- Infant Feeding With and Without Added Carbohydrate. L. E. Harris.—p. 677.
- Factors Affecting Retention of Nitrogen and Calcium in Period of Growth: IX. Corticotropin (ACTH). J. A. Johnston and M. J. Sweeney.—p. 685.
- Relation Between Socioeconomic Status and Body Size in Boys 7 to 10 Years of Age. H. V. Meredith.—p. 702.

Treatment of Tuberculosis.—Various tuberculostatic agents were used in treatment of 172 children in the tuberculosis ward of Bellevue Hospital, New York, during the last four and one-half years. It was found that streptomycin should be used in treatment of meningitis, miliary tuberculosis, protracted hema-

togenous tuberculosis, progressive primary tuberculosis with cavitation and bronchogenic spread, and progressive advanced chronic pulmonary tuberculosis. In meningitis it should be administered by both intrathecal and intramuscular routes. Streptomycin may be used to treat nonfatal complications of tuberculosis, but this measure should always be weighed in relation to the expected response to other measures and to the possible future needs for streptomycin for other forms of tuberculosis. Streptomycin should be considered contraindicated in uncomplicated, asymptomatic primary tuberculosis regardless of the age of the child or extent of the primary complex, because it has not been shown to effect rapid cure of the primary form or to prevent complications and also because of danger of development of tubercle bacilli resistant to streptomycin, thus preventing effective use of the drug in the event of a serious complication. Combined therapy is indicated whenever streptomycin therapy is continued for more than three weeks, because it delays development of resistance to streptomycin and the effect of each drug is enhanced by the combination. Thiazolsulfone was used with streptomycin when control of lymphohematogenous tuberculosis was the main problem, and *p*-aminosalicylic acid was used with streptomycin for progressive primary or reinfection tuberculosis. With the exception of exfoliative dermatitis in one patient, no severe toxic reaction to streptomycin administered intramuscularly has been observed. Vestibular function is disturbed in almost every case, but this effect is apparently reversible. Deafness occurred only in patients with tuberculous meningitis treated with streptomycin intrathecally and was not reversible. Toxic reactions to streptomycin given intrathecally were never severe enough to require discontinuance of treatment. Toxic reactions to thiazolsulfone were not troublesome. *p*-Aminosalicylic acid is well tolerated by children in proper dosage.

Allergic Dermal-Respiratory Syndrome.—Ratner and collaborators define the allergic dermal-respiratory syndrome as a symptom complex in which both dermal (urticaria, eczema) and respiratory (perennial rhinitis, hay fever, asthma) manifestations of allergy occur in the same patient, either concurrently or at different periods. They analyzed data from 750 cases seen in clinic and private practice over a number of years, and found that 35% of allergic children have both dermal and respiratory manifestations. More than half of the children (59%) with eczema later had respiratory allergy, asthma more often than hay fever. The authors confirmed the generally accepted view that eczema in childhood almost always begins during the first year of life. Asthma nearly always appears before the age of 8 years and in the majority of cases before the age of 4. The onset of hay fever usually occurs before the seventh year. Three stages in the evolution of the dermal-respiratory syndrome are described: Stage 1 is characterized by dermal manifestations, absence of respiratory symptoms, and negative skin reactions to inhalants, and is present chiefly in infants. In one form of stage 2 there are dermal manifestations, no respiratory symptoms, and positive skin reactions to inhalants. In another form of stage 2 there are both dermal and respiratory manifestations and negative skin reactions to inhalants. Stage 3 is characterized by dermal and respiratory symptoms and positive skin reactions to inhalants and occurs almost entirely in older children. Eczema in infancy and childhood should not be regarded solely as a dermatological condition. Every case of dermal allergy should be viewed as a potential case of asthma or hay fever.

American Journal of Clinical Pathology, Baltimore

21:1101-1202 (Dec.) 1951. Partial Index

- Differential Test for Infectious Mononucleosis. I. Davidsohn, K. Stern and C. Kashiwagi.—p. 1101.
- Isolation of Pathogens from Tissues of Embalmed Human Bodies. L. A. Weed and A. H. Baggenstoss.—p. 1114.
- Seasonal Variation in Pregnancy Test Using Rana Pipiens. J. B. Holyoke and E. E. Hoag.—p. 1121.
- Critique of Methods for Determination of Protein in Cerebrospinal Fluid. H. L. Wikoff and P. Kazdan.—p. 1173.

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Titles marked with an asterisk (*) are abstracted.

American J. Digestive Diseases, Fort Wayne, Ind.

18:349-382 (Dec.) 1951

- Diabetes Mellitus and Concomitant Leukemia. J. T. Paul, W. R. Best and L. R. Limarzi.—p. 349.
- Achylia Gastrica: Keystone in Development and Eradication of Macrocytic Achylic Anemia (Pernicious Anemia, Addison-Biermer). F. S. Weinberg.—p. 351.
- Effect of Lysozyme Inactivating Anion Exchange Polymer in Treatment of Peptic Ulcer: Experimental and Clinical Study. I. J. Greenblatt, M. Jacobi and T. D. Cohen.—p. 362.
- Nutritional Substitution Therapy: New Method Which Prevents Prostatic Surgery in Benign Physiological Hypertrophy: Preliminary Report. B. F. Sieve.—p. 369.

American Journal of Hygiene, Baltimore

54:295-440 (Nov.) 1951

- *Vaccination of Human Beings Against Mumps: Vaccine Administered at the Start of Epidemic: I. Incidence and Severity of Mumps in Vaccinated and Control Groups. K. Habel.—p. 295.
- Id.: II. Effect of Vaccination upon Epidemic. K. Habel.—p. 312.
- *Q Fever in California: XI. Epidemiologic Summary of 350 Cases Occurring in Northern California During 1948-1949. W. H. Clark, E. H. Lennette and R. S. Romer.—p. 319.
- Antistreptolysin "O," Antihyaluronidase and Streptococcal Agglutinin Titers in Seventh and Eighth Grade School Children from Two Connecticut Cities: Serological and Environmental Study. R. W. Quinn, S. J. Quinn and P. Quinn.—p. 331.
- Factors in Agglutination Reaction, and the Relationship between Agglutination Activity and Toxicity of Toxin Preparations. J. P. Lowenthal and C. Lamanna.—p. 342.
- Social Serology: Antibody Levels in Normal Young Population During Epidemic of Poliomyelitis. J. L. Melnick and N. Ledinko.—p. 354.
- Isolation of Coxsackie Virus (C Virus) from North Alaskan Eskimos. D. D. Banker and J. L. Melnick.—p. 383.
- Complement-Fixation Test for Lansing Strain of Poliomyelitis Virus. O. Lahelle.—p. 391.
- Observations on Habits, Ecology and Life Cycle of Oncomelania Nosophora, Molluscan Intermediate Host of Schistosoma Japonicum in Japan. D. B. McMullen, S. Komiyama and T. Endo-Itabashi.—p. 402.
- Seasonal Studies of Schistosoma Japonicum in Intermediate Host, Oncomelania Nosophora. D. B. McMullen, T. Endo-Itabashi, S. Seto and others.—p. 416.
- Report of Isolated Outbreak of Influenza Type B, Camp Haugen, Japan, 1950. K. F. Burns and A. P. Long.—p. 431.

Mumps Vaccination.—The effects of prophylactic immunization of human beings against mumps were studied in 2,825 Negroes who in 1946 were brought from Barbados to work on sugar plantations in Florida. Past experience showed that these Negroes are highly susceptible to mumps. The workers were from 16 to 50 years of age, in good health, and had no previous history of mumps. They were housed in nine camps on Lake Ocheechobee and their contacts with the population of the area were few. One dose of chick-embryo inactivated mumps vaccine mixed with a peanut oil-beeswax adjuvant was administered to 1,344 men at the time of the first wave of infection. The others served as controls. All patients had approximately equal susceptibility to mumps, as indicated by a virus neutralization test performed in the chick-embryo with serum of all men before vaccination. This test also gave good correlation between actual immunity and the presence of antibody of this type. The incidence of mumps in control and vaccinated groups was about equal for the first three weeks, after which it began to increase in the control group, the ratio becoming 2 to 1 after the third week and 3 to 1 after the sixth. A total of 383 men received a second dose of vaccine six weeks after the first vaccination. Although its increased prophylactic effect could not be demonstrated because of the small number of cases occurring after this dose was given, the level of serum antibodies was higher than that which is usually observed in convalescence from mumps. Clinical manifestations of mumps in vaccinated persons were definitely milder than those in unvaccinated persons, and complications were fewer. No allergy or local reaction to the vaccine was observed. Information as to the duration of the immunity produced by the vaccine is not available.

Q Fever in Northern California.—Epidemiological studies in 350 cases of Q fever that occurred in Northern California during 1948-1949 showed that 292 of the patients were from 20 to 59 years of age and that only 32 were women. Most of the cases occurred in an area of intense agricultural, dairying, and stock-raising activity (Central Valley of California) during the months following the seasonal peak of sheep-raising operations (March,

April, and May). Contact with an ill person, contaminated food or water, and ticks or other blood-sucking arthropods were never responsible for the infection. Of the patients, 242 had had contact with livestock, their products, or environment, while 84 had had no known contact with the presumed sources of infection. However, in the agricultural areas where the cases occurred a degree of casual contact with livestock is common. Studies of serum antibodies in normal persons of the principal endemic area showed that the proportion of positive reactions was higher than in normal persons from two nonendemic areas. Antibodies of this type were found in 5.1% of men from the endemic area who were not ill but in only 1.8% of women from the same area who were not ill. The source of infection and the mode of transmission of Q fever have not as yet been clearly defined. Direct contact with the excreta or tissues of an infected animal may result in infection, and the infective agent may enter the body of the host through the respiratory or digestive tracts. Further studies are needed to test the hypothesis that rickettsiae are disseminated by air from contaminated environments.

American Journal of Obstetrics & Gynecology, St. Louis

62:947-1186 (Nov.) 1951. Partial Index

- *Studies on Iron Deficiency Anemia of Pregnancy: Including Plasma Volume, Total Hemoglobin, Erythrocyte Protoporphyrin in Treated and Untreated Normal and Anemic Patients. C. J. Lund.—p. 947.
- *Clinical Evaluation of Silver Carbonate Vaginal Smear Method in Diagnosis of Cancer. G. M. Riley, J. S. Behrman, A. Arcilla and E. Dontas.—p. 985.
- Cyclic Variations in Endocervix. G. B. Bradburn and C. F. Webb.—p. 997.
- Nutrition and Premature Labor. H. Speert, S. Graff and A. M. Graff.—p. 1009.
- Retinal Changes in Toxemias of Pregnancy: I. History, Vomiting of Pregnancy, Mild and Severe Pre-Eclampsia, and Eclampsia. R. Landesman, R. G. Douglas and S. S. Snyder.—p. 1020.
- Lesions of Vaginal Vault Following Complete Hysterectomy. R. A. Beebe and E. A. Edwards.—p. 1034.
- True Sacculization of Contracture Portion of Pregnant Uterus. W. H. Rubovits.—p. 1044.
- Acute Renal Insufficiency: Physiopathology and Treatment, with Presentation of Cases Occurring on Obstetric Service. H. D. Priddle and C. S. Stevenson.—p. 1053.
- Responsibility of Obstetrician to Fetus: I. Analysis of Fetal and Neonatal Mortality in 10,000 Deliveries. J. W. Simpson and L. J. Geppert.—p. 1062.
- Feminizing Ovarian Tumors and Pregnancy. A. W. Diddle and K. A. O'Connor.—p. 1071.
- Mistakes in Interpretations of Intraepithelial Carcinoma. E. R. Novak and G. A. Galvin.—p. 1079.
- Relationship of Prolonged Labor to Fetal Mortality. G. W. Corner Jr., R. W. Kistner and R. L. Wall.—p. 1086.
- Use of New Veratrum Preparations in Treatment of Toxemia of Pregnancy. W. W. Baird and N. S. Assali.—p. 1093.
- Cyclic Biochemical Changes in Human Endometrium, with Special Reference to Fibrinolytic Enzyme. E. W. Page, M. B. Glendenning and D. Parkinson.—p. 1100.
- Care of Postpartum Cervix. A. E. Weiner and H. B. Nelson.—p. 1106.
- Vaginal Hysterectomy. R. T. Weaver and F. L. Johnson.—p. 1117.
- Suppression of Lactation with Stilbestrol. D. G. Morton and J. S. Miller.—p. 1124.
- Intravenous Procaine-Pentothal During Labor: Preliminary Report. S. Belinkoff and G. Trudeau.—p. 1129.

Iron Deficiency Anemia in Pregnancy.—The capillary hemoglobin level was determined in 4,015 women at their first visit to the prenatal clinic of the Charity Hospital of Louisiana in New Orleans. Approximately 20% had hemoglobin values below the minimum of 10 gm. per 100 cc. considered normal during pregnancy. If the more accurate minimum of 11 gm. per 100 cc. is used, 50% of the patients were anemic. Complete studies were done on 66 patients during 402 outpatient examinations. These patients were divided into two major categories, those who were normal and those who had iron deficiency anemia. Each of these groups was further subdivided on the basis of iron therapy. Of the 21 normal pregnant women who served as controls, seven were treated with molybdenized ferrous sulfate, 6 grains (0.37 gm.) three times a day, and the other 14 were not treated. Of the 45 women with iron deficiency, 10 were not treated at first, but 5 of these had to be treated before delivery. Newer biochemical techniques, including determination of blood volume and free erythrocyte protoporphyrin, were used in conjunction with routine hematologic mensuration throughout pregnancy. Total plasma volume increased progressively, reaching a broad peak between the 28th and 38th weeks of gestation. The

increases were orderly in individuals but the variations between individuals were extreme, ranging from 14 to 121%. Calculation of total hemoglobin mass eliminated the effect of variations in the plasma volume. The total hemoglobin mass increased progressively during apparently normal pregnancy, reaching a peak elevation of about 15% at term. If the normal controls were treated with iron there appeared to be an even greater increase in total hemoglobin. With or without therapy, the total hemoglobin level declined to the original level by the eighth week post partum. If untreated, the iron deficiency anemia becomes severer as pregnancy progresses. Rapid or excessive change in plasma volume will mask or exaggerate the response to iron therapy when interpreted by routine blood counts. Calculation of total hemoglobin shows the true response. The oral administration of a molybdenum ferrous sulfate compound was effective in treatment of 95% of the patients with iron deficiency anemia of pregnancy.

Silver Carbonate Vaginal Smear Method.—Riley and associates point out that with few exceptions those attempting to evaluate the so-called "cytological method" of cancer diagnosis have employed the Papanicolaou technique. In 1948 Riley and associates reported that exfoliated cells, as found in the vaginal smear, were readily impregnated with silver carbonate solution prepared according to the method of Del Rio Hortega. The chromatin material was remarkably argyrophilic. It was emphasized that, since the chief evidences of malignant growth were nuclear aberrations, a distinctive nuclear stain would be most desirable. Technical aspects of the method have been thoroughly investigated, and it has been given a rigorous clinical trial. The authors describe the technical details of the silver carbonate staining method for vaginal smears and illustrate the qualities of the stain by photomicrographs of normal, suspicious, and malignant cells. During the years 1947 to 1950, three different examiners evaluated smears from a total of 2,008 gynecological patients whose history or clinical findings suggested carcinoma of the uterus. The total number of carcinoma cases in the series was 120. Of this number, 98 carcinomas were correctly diagnosed, and 22 (18%) were undetected. In the 1,888 patients without pathologically diagnosed carcinoma, 22 false positive diagnoses (1.2%) were submitted. The total percentage error based on the total number of cases studied was 2.2%. Thus the accuracy of this procedure compares favorably with that reported by others using conventional polychrome stains. The silver technique has the practical advantages over polychrome procedures of simplicity, rapidity, ease of examination, and the facility with which nuclear aberrations are recognized. These qualities, together with the observed accuracy, should prove of value in the application of cytological methods for the detection of carcinoma.

American Journal of Pathology, Ann Arbor, Mich.

27:925-1130 (Nov.-Dec.) 1951

- Evolution of Rheumatoid Nodules Treated with Cortisone and of Non-Treated Rheumatoid Nodules. R. Fienberg and F. L. Colpoys Jr.—p. 925.
- *Pathogenesis of Cirrhosis Produced by Choline Deficiency: Escape of Lipid from Fatty Hepatic Cysts into Biliary and Vascular Systems. W. S. Hartroft and J. H. Ridout.—p. 951.
- Inflammation and Repair of Glomerulus. D. B. Jones.—p. 991.
- Histochemical Detection of Fatal Anticholinesterase Poisoning. A. D. Bergner and S. H. Durlacher.—p. 1011.
- Association of Iron-Containing Crystals with Schaumann Bodies in Giant Cells of Granulomas of Sarcoid Type. R. L. Engle Jr.—p. 1023.
- Affinity of Fibrinoid Substances for Acid Dyes. L. Sokoloff, A. Mund and T. G. Kantor.—p. 1037.
- Morbid Anatomy of Experimental Cocksackie Virus Infection. R. Gifford and G. Dalldorf.—p. 1047.
- Virus-Induced Mitosis in Adult Nerve Cells of Rabbit Retina. J. R. Overman and H. Dorch Jr.—p. 1065.
- Experimental Transmission of Cutaneous Papilloma of Horse. R. H. Cook and C. Olson Jr.—p. 1087.

Cirrhosis Produced by Choline Deficiency.—In a previous report the structure, formation, and involution of pathologic fatty cysts (lipodiastemata) in the livers of rats fed a diet low in choline were reported. The manner in which lipid escapes from fatty cysts is described in this paper. Cysts may rupture into either a bile canaliculus or a hepatic sinusoid. In the first instance the fat released from the cyst escapes into the biliary tree and may

be demonstrated within the lumina of bile canaliculi and ducts. In the second case fat droplets enter the vascular system. Droplets of stainable fat are found as emboli in the vessels of the heart, lungs, and kidneys. The morphologic changes in the red blood cells found in ruptured fatty cysts suggest that the erythrocytes may become closely bound to ceroid so that they are often indistinguishable from other deposits of this pigment. The trabeculation in experimental dietary cirrhosis represents a condensation rather than a proliferation of the preexistent stroma. The bile passages in the trabeculae may be derived to a large extent from cysts that have ruptured into biliary canaliculi. Frozen sections of livers, kidneys, and lungs from 30 patients with alcoholism were examined, and cysts were identified in every case in which fatty cirrhosis was in an active stage. Small amounts of embolic fat within the vessels of both lungs and kidneys were detected in a number of cases. These findings suggest that a sequence of pathologic changes similar to those described for choline-deficient rats may occur in the cirrhosis associated with excessive intake of alcohol by human subjects. In the choline-deficient rats it appeared that accumulation of excess fat within cysts in the liver was the primary etiologic factor, which in turn caused secondary fibrosis and nodular hyperplasia.

American Journal of Physiology, Baltimore

167:289-558 (Nov.) 1951. Partial Index

- Muscle Electrolytes in Rats Following Ischemia Produced by Tourniquets. F. A. Fuhrman and J. M. Crismon.—p. 289.
- Acute KC1 and Histamine Tolerance and Adrenal Weight in X-Irradiated Mice. W. W. Smith.—p. 321.
- Sodium and Potassium of Blood and Urine in Adrenalectomized Golden Hamsters. J. G. Snyder and L. C. Wyman.—p. 328.
- Effects of Cortisone and DCA on Radiosodium Transport in Normal and Adrenalectomized Dogs. R. R. Overman, A. K. Davis and A. C. Bass.—p. 333.
- Survival of Adrenalectomized Rats With and Without Replacement Therapy Following X-Irradiation. A. Edelmann.—p. 345.
- Effects of Thyroxine, 3, 5-Diiodothyronine and Thyronine on Ascorbic Acid Oxidation. C. L. Gemmill.—p. 349.
- Tolerance of Normal and Alloxan-Treated Rats to Intravenous Glucose and Glucose-1-Phosphate. C. A. Kuether.—p. 355.
- Does Concentration of Glucose in Extracellular Fluid Influence Its Utilization by Tissues? A. N. Wick and D. R. Drury.—p. 359.
- Ammonia and Urea Production and Changes in Absorption Spectra of Nucleic Acid Derivatives Following Ultraviolet Irradiation. A. Canzanelli, R. Guild and D. Rapport.—p. 364.
- Calorie Intake and Fertility in C57H-Male Mice. Y. Ching Puh Lee, J. T. King and M. B. Visscher.—p. 375.
- Correlation Between Propulsive Motility and Length of Small Intestine in Albino Rats and Dogs. J. C. Stickney, E. J. Van Liere and D. W. Northup.—p. 399.
- Chylomicra: Their Composition and Their Fate After Intravenous Injection of Small Amounts of Heparin. R. L. Swank and V. Wilmot.—p. 403.
- Local and General Alterations of Blood CO₂ and Influence of Intestinal Motility in Regulation of Intestinal Blood Flow. M. S. Mohamed and J. W. Bean.—p. 413.
- Arterial, Atrial and Venous Pressure Changes in Presence of Arterio-venous Fistula. J. L. Nickerson, F. W. Cooper Jr., R. Robertson and J. V. Warren.—p. 426.
- Electrocardiographic Effects of Reflex Vagal Stimulation. J. C. Scott and E. A. Reed.—p. 441.
- Depressor Effect of Potassium Deprivation on Blood Pressure of Hypertensive Rats. M. Friedman, R. H. Rosenman and S. C. Freed.—p. 457.
- Water Diuresis in Salt-Depleted Dog. L. J. Cizek and K. C. Huang.—p. 473.

American Journal of Public Health, New York

41:1455-1572 (Dec.) 1951

- International Health—A Symposium. C. E. A. Winslow and others.—p. 1455.
- Recent Developments in Prophylaxis of Rabies. H. Koprowski and H. R. Cox.—p. 1483.
- Study on Etiology, Epidemiology, and Antibiotic Therapy of Infantile Diarrhea, with Particular Reference to Certain Serotypes of Escherichia Coli. E. Neter, C. R. Webb, C. N. Shumway and M. R. Murdock.—p. 1490.
- Role of the School of Public Health in Meeting Man Power Crisis. H. F. Vaughan.—p. 1497.
- The Most Important Thing. F. A. Gibbs.—p. 1503.
- Conservation of Hearing Program for School Children: Review of Three Year Experience in Harford County, Maryland. C. R. Hayman, B. S. Rich and E. Stark.—p. 1509.
- Preliminary Report of Histoplasmin and Other Antigen Sensitivity in North Carolina. R. J. Murphy, W. M. Peck and B. Vincent.—p. 1521.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

66:873-1064 (Dec.) 1951

- Some Thoughts on Training of Radiation Therapist. Janeway Lecture, 1951. H. D. Kerr.—p. 873.
- Symmetrical Calcifications in Anterior Limb of Internal Capsules of Brain Without Demonstrable Neurological or Metabolic Disturbances. J. F. Sammet and P. C. Bucy.—p. 880.
- Advanced Atrophy and Enlargement of Sella Turcica with Destruction of Sphenoid. B. S. Epstein and L. M. Davidoff.—p. 884.
- Cor Pulmonale Resulting from Pulmonary Arteriosclerosis: Report of Case. J. S. Wells and P. Brown.—p. 894.
- Pulmonary Metastatic Sarcoma with Associated Pneumothorax: Report of Two Cases. T. F. Leigh and E. A. Thompson.—p. 900.
- Pathology and Classification of Tumors of Soft Tissues. A. P. Stout.—p. 903.
- *Brucella Infection of Bones and Joints. C. N. Ploussard.—p. 910.
- Premalignant Lesions of Gastrointestinal Tract: I. Significance of Roentgenologic Evidence of Hypertrophic Gastritis. R. P. Barden.—p. 915.
- *Glycogen Disease: Report of Two Cases with Cardiomegaly. J. F. Martin and F. J. Bonte.—p. 922.
- Practice of Radiology in the United States: Facts and Figures. S. W. Donaldson.—p. 929.
- Roentgen Treatment of Cervical Spondylosis: Follow-Up Examination of 625 Patients. J. Lundar.—p. 947.
- Directed Beam Therapy: Rotational Therapy Chair. B. V. A. Low-Beer.—p. 956.
- Comparison of Three Survey Instruments Exposed to Various Radiations. R. F. Cowing, E. DeAmicis and C. K. Spalding.—p. 961.
- Balanced Chest Roentgenography. I. J. Kane and S. Heiser.—p. 967.

Brucella Infection of Bone and Joints.—The occurrence of brucellosis involving the hip joint is reported in a man, aged 37, who had wrenched his left hip while moving heavy machinery. Three months after his injury roentgenograms of the hip showed destruction of bone and joint cartilage, and the agglutination reaction for *Brucella abortus* was positive in all dilutions with purified protein derivative. The hip was immobilized in a cast. Roentgenographic diagnosis of the condition was made five months after injury, when the anteroposterior view showed a beginning infectious process of the hip. Two months later the cast was removed and the roentgenogram revealed that the arthritis of the hip caused by undulant fever was healed. Additional roentgenograms taken three and a half months later showed an area in the upper third of the shaft of the femur indicative of bone infection, although the infection in the head of the femur had completely healed. The agglutination reaction was still positive for *Brucella abortus*. Roentgenographic examination fifteen months after injury showed complete healing of the infectious process in the hip joint, and the area in the upper third of the shaft of the femur had practically disappeared.

Glycogen Disease.—The cardiac form of glycogen storage disease in two infants, aged five months and nine weeks, respectively, is reported. Roentgenograms of the chest were taken in both cases, and angiocardiology was used in one. The roentgenographic studies were of value in demonstrating enlargement of the heart and secondary changes in the adjacent structures, such as displacement and narrowing of the trachea, narrowing of the left main stem bronchus, and atelectasis of the upper lobe of the left lung. Angiocardiology demonstrated normal circulation of the contrast medium through the heart and great vessels. The chambers of the heart were slightly enlarged, and the left ventricular wall was moderately thickened, probably indicating that hypertrophy was a more prominent factor in the enlargement than dilatation of the chambers. Both patients died and necropsy was performed. It revealed pronounced deposition of glycogen in the myocardium of the older patient; the heart was pale and thickened and weighed 185 gm. compared to an expected weight of 31 gm. The wall of the left ventricle was 10 mm. thick and the right ventricle 3 mm. The liver was moderately enlarged, and glycogen deposits were seen within its cells. In the other patient the heart was bright red and appeared uniformly enlarged, with a weight of 90 gm. compared to an expected weight of 23 gm. The right ventricular wall was 4 mm. thick, while the left ventricular wall measured 7 mm. The endocardium revealed pronounced fibrosis, particularly in the left ventricle. The liver was not enlarged. Glycogen disease is uncommon, but is important enough to be considered in the differential diagnosis by roentgenograms of enlargement of the liver, heart, and kidneys during infancy and childhood. Clinical diagnosis of the cardiac form of glycogen disease is difficult because of the lack of diagnostic laboratory tests. Clinical

observations, routine laboratory procedures, roentgenoscopy, and electrocardiography do not permit differentiation of certain congenital defects, idiopathic hypertrophy, rhabdomyoma, and glycogen storage disease. On the basis of their experience in these two cases, the authors stress the value of roentgenographic studies in glycogen disease, one of the causes of cardiac enlargement in the first year of life. They emphasize the use of angiocardiology in excluding congenital anomalies and in the evaluation of hypertrophy and dilatation. The final differential diagnosis must depend on demonstration of an increased glycogen content in the skeletal muscle obtained at biopsy or on evidence of some abnormality of carbohydrate metabolism.

Am. J. Syphilis, Gonorrhea and Ven. Dis., St. Louis

35:503-620 (Nov.) 1951

- Electron Microscope Studies of Treponemes: III. Flagella. H. E. Morton, G. Rake and N. R. Rose.—p. 503.
- Cortisone in Interstitial Keratitis. A. C. Woods.—p. 517.
- Effect of Local Cortisone in Treatment of Syphilitic Interstitial Keratitis: Preliminary Report. G. W. Crane Jr. and S. D. McPherson Jr.—p. 525.
- Estimates of Relapse and Reinfection Rates in Early Syphilis Treated with Penicillin. M. Merrell.—p. 532.
- *Oral Treatment of Neurosyphilis with Aureomycin: Progress Report. R. R. Kierland and P. A. O'Leary.—p. 544.
- Comparison of Results of Spinal Fluid Examination by Two Separate Laboratories on Duplicate Specimens of Spinal Fluid from 400 Patients with Syphilis. W. T. Ford, J. H. Stokes, H. Beerman and C. J. Gentzkow.—p. 553.
- *Treatment of Neurosyphilis: One- to Six-Year Follow-Up of Patients Treated with Penicillin at the Boston Psychopathic Hospital—Comparison of Results with Penicillin Alone and Combined Penicillin-Malaria Therapy. V. P. Perlo, A. S. Rose, L. R. Carmen and H. C. Solomon.—p. 559.
- Further Attempts to Immunize Rabbits with Killed *Treponema pallidum*. G. W. Waring Jr. and W. L. Fleming.—p. 568.
- Role of Sitilopin in Serologic Tests for Syphilis. C. R. Rein, L. C. Kelcey and T. M. Rosenfield.—p. 573.
- Reactions to Penicillin. D. K. Kitchen, C. R. Rein, E. W. Thomas and H. J. Spoor.—p. 578.
- Treatment of Inclusion Urethritis, Including One Case of Reiter's Disease, with Chloramphenicol. G. M. Findlay and R. R. Willcox.—p. 583.

Treatment of Neurosyphilis with Aureomycin.—Results of treatment with aureomycin are described in 10 of 12 previously reported cases of neurosyphilis that were observed for from 573 to 122 days (average 409 days) and in 9 additional cases. While the dosage of aureomycin varied considerably, it still seems that approximately 60 gm. of aureomycin, with 2 to 4 gm. given daily in divided doses, is sufficient for a single or first course of therapy. Early clinical improvement following treatment with aureomycin continued although less rapidly. The greatest clinical benefit appeared within the first 6 to 10 months after treatment was begun. In no case of asymptomatic neurosyphilis did symptomatic neurosyphilis develop. All but one patient with symptomatic neurosyphilis showed moderate to pronounced improvement in their specific syphilitic symptoms. Weight gain and an increased sense of well-being were noted in these as well as in penicillin-treated patients. As time went on it appeared that the early benefits from aureomycin were extended and maintained. The results of aureomycin therapy equalled those of penicillin in these 19 cases of neurosyphilis. Aureomycin may be used for patients with neurosyphilis who are resistant or hypersensitive to penicillin.

Follow-Up of Neurosyphilitic Patients Treated with Penicillin.—Of 469 patients with neurosyphilis treated with penicillin between February, 1944, and January, 1950, 66 patients died. In 33 of these general paresis was a contributory cause of death. Thirty-eight patients were either lost to observation or had been followed for less than one year. Of the remaining 365 patients, followed for one to six years, 116 (32%) were treated with 3,000,000 to 9,000,000 units of penicillin alone, while 249 were given penicillin and modified malaria or fever cabinet therapy. Re-treatment was necessary in 31 patients (26%) who received penicillin alone and in 42 patients (17%) who received combined treatment. Of the entire group of 365 patients, 72% of whom had general paresis or taboparesis, 211 (58%) showed clinical improvement, 204 (56%) were gainfully employed, and 208 (57%) made a good or fair social adjustment. In the 116 patients treated with penicillin alone, the symptoms of 80 (69%) were improved, those of 17 (15%) were arrested, and those of 19

(16%) were worse or unchanged. In the 249 patients who received combined treatment, the symptoms of 131 (53%) were improved, of 57 (23%) were arrested, and of 61 (24%) were worse or unchanged. Thus over-all results in patients treated with penicillin alone were distinctly superior to those obtained with combined treatment. This probably reflects the fact that in mild cases treatment was usually with penicillin alone, while in severe cases combined treatment was given. However, in a group of patients judged before treatment to have comparatively severe dementia paralytica, clinical results with penicillin alone proved slightly more favorable than those obtained with combined treatment. The usual pattern of spinal fluid improvement during the first year after treatment was obtained with both methods of treatment. Late spinal fluid examination revealed normal or near normal fluids in 71% of patients receiving combined treatment, compared with 60% of those treated with penicillin alone. On the basis of a six year follow-up period, penicillin alone appears to be as effective as combined penicillin-fever treatment for all forms of neurosyphilis. Final evaluation of results with penicillin alone requires a longer follow-up period than is presently available.

American Review of Tuberculosis, New York

64:583-716 (Dec.) 1951

- Cardiopulmonary Function in Hematogenous Pulmonary Tuberculosis in Patients Receiving Streptomycin Therapy. J. H. McClement, A. D. Renzetti Jr., D. Carroll and others.—p. 583.
- Extraction and Fractionation of Water-Soluble Components from Tubercle Bacilli. R. J. Heckly and D. W. Watson.—p. 602.
- *Pulmonary Tuberculosis, Bronchiectasis, and Calcification as Related to Bronchogenic Carcinoma. C. E. Woodruff and H. C. Nahas.—p. 620.
- *Adrenocortical Function in Pulmonary Tuberculosis. A. J. Finestone and C. R. Shuman.—p. 630.
- Complications of Artificial Pneumoperitoneum: Review. H. F. Stein.—p. 645.
- Experimental Studies on Toxicity of Amithiozone in Dogs. J. H. Moyer and R. B. Perkins.—p. 659.
- Tuberculostatic Serum Substance Possessing Lysozyme-Like Properties. Q. Myrvik and R. S. Weiser.—p. 669.
- New Serologic Test for Tuberculosis: Preliminary Report. E. R. Maillard and F. J. Gagliardo.—p. 675.

Bronchiectasis and Bronchogenic Carcinoma.—Of 23 men between the ages of 42 and 87 with bronchogenic carcinoma, 12 had squamous cell carcinoma identified microscopically by epithelial pearls. All 12 of these tumors were found in an upper lobe; all but 1 were associated with large calcified foci in the same lobe or in the adjacent tracheobronchial lymph nodes; and all but 2 were not associated with active tuberculosis. The anatomic findings associated with other types of lung tumors were quite different. An important associated etiological factor in bronchogenic carcinoma may be healed tuberculosis that has left an area of bronchiectasis in the lungs and a calcified focus in the adjacent lymph nodes. Evidently a person in the "cancer age" might have smoked for many years with little danger of developing pulmonary malignancy if there were no associated bronchiectasis. On the other hand there would be little danger of malignant change in a person with bronchiectasis if he did not smoke. The presence of both bronchiectasis and inveterate smoking compounds the chances of malignancy developing in the lung. It should be recognized that calcified tracheobronchial lymph nodes may be particularly susceptible to development of malignant disease.

Adrenocortical Function in Pulmonary Tuberculosis.—Adrenocortical function was studied in 50 patients with pulmonary tuberculosis by means of the eosinophil test of Thorn and the hyaluronidase-fluorescein skin test. The adrenal cortex was stimulated by 0.3 cc. of 1:1,000 epinephrine injected subcutaneously in 46 patients. In the remaining four patients the alarm stimulus was thoracoplasty. The factors considered in clinical evaluation were the toxicity, chronicity, and clinical course at the time adrenocortical function was measured. In general, there was good correlation between the results of the tests. Eosinophil responses to epinephrine or surgical intervention were normal in 16 patients, while responses were inadequate in 23 patients. In the remaining 11 patients the initial fasting eosinophil count was too low for this test to be valid. There appeared to be no definite relationship between the adequacy of the eosinophil responses and the toxicity, chronicity, or clinical state of the

patient. Nine patients had normal adrenal cortical function as measured by the hyaluronidase-fluorescein skin test. The initial disappearance of the hyaluronidase-fluorescein wheal was delayed in seven patients but was further inhibited after adrenocortical activation. The latter group may represent cases with some degree of hyperadrenocorticism. Failure of adrenocortical stimulation to inhibit the disappearance of the wheal occurred in 12 patients, while 22 patients showed a prolonged initial disappearance time of the skin wheal with inadequate inhibition after adrenocortical activation. This suggests that the patients in the latter group had a degree of adrenocortical activity that could not be increased by further stress. There appeared to be no definite correlation between the degree of toxicity and chronicity and the response to the hyaluronidase-fluorescein skin test. No definite conclusions can be made about the relation of the clinical course to the results of the skin test. Ten of the 17 patients who were improving had inadequate adrenocortical responses as measured by this test. Results of the authors' study demonstrated that in pulmonary tuberculosis adrenocortical function is altered, but the exact nature of this change could not be determined.

Annals Otol., Rhin. and Laryngology, St. Louis

60:591-894 (Sept.) 1951. Partial Index

- Intracranial Division of Eighth Nerve for Ménière's Disease: Follow-Up Study. R. E. Green and C. C. Douglass.—p. 610.
- Temporal Lobe Herniation: Through Traumatic Defect in Tegmen of Temporal Bone with Cerebrospinal Otorrhea. W. F. Andrew.—p. 622.
- Erosion of Esophagus by Intrathoracic Goiter. M. Davidson and J. L. Turner.—p. 631.
- *Treatment of Acute Suppurative Otitis Media: Relative Merits of Chemotherapy and Myringotomy in Avoiding Surgical Mastoiditis. M. G. Evans.—p. 638.
- Surgery in Ménière's Disease: New Operation Which Preserves the Labyrinth: Report of Cases. S. Rosen.—p. 657.
- Treatment of Endolymphatic Hydrops (Ménière's Disease) with Streptomycin. H. V. Hanson.—p. 676.
- Congenital Anomalies of Esophagus. P. H. Holinger, K. C. Johnston and W. J. Potts.—p. 707.
- Follow-Up Observations on Treatment of Benign Stenosis of Esophagus. G. Tucker and H. R. Hawthorne.—p. 731.
- Superior Vena Caval Obstructive Syndrome: Report of Three Cases. W. A. Lell.—p. 754.
- Laryngeal Sequelae of Endotracheal Anesthesia. S. H. Baron and H. W. Kohlmoos.—p. 767.
- Obscure Pulmonary Bleeding. J. J. Hennessy.—p. 819.
- Primary Tuberculoma of Bronchus. J. J. O'Keefe.—p. 824.
- Application of Streptomycin in Tuberculous Bronchitis. A. R. Judd.—p. 828.
- Cytologic Studies and Prognostic Results in Bronchogenic Carcinoma. L. H. Clerf, P. A. Herbut and T. F. Nealon Jr.—p. 840.
- Tracheal Resection with Primary Anastomosis. E. B. Kay.—p. 864.

Chemotherapy and Myringotomy in Acute Suppurative Otitis Media.—Evans reviews clinical, laboratory, and operative findings in 30 patients admitted to the Massachusetts Eye and Ear Infirmary with acute mastoiditis requiring mastoidectomy, and in 45 patients with acute suppurative otitis media treated in the outpatient department by myringotomy. All of the outpatients treated by myringotomy recovered without mastoidectomy. Of the 30 patients hospitalized with acute mastoiditis, all but two had received chemotherapy prior to admission but not one had had a paracentesis. In these patients 36 mastoidectomies were required to eradicate the disease. On the basis of these observations and from a review of the literature, the author concludes that the low incidence of surgical mastoiditis in the past few years is due to the low incidence of acute suppurative otitis media rather than to the routine use of chemotherapeutic and antibiotic agents. The role of chemotherapy in preventing surgical mastoidectomy is, at best, secondary or adjuvant. Myringotomy is necessary in the early treatment of acute suppurative otitis media whether or not chemotherapeutic or antibiotic agents are used.

Arkansas Medical Society Journal, Fort Smith

48:129-150 (Nov.) 1951

- Intraocular Foreign Bodies: Localization and Surgical Treatment. G. H. Landers and G. C. Burton.—p. 129.
- Erythroblastosis Fetalis (Hemolytic Disease of Newborn). W. F. Mengert.—p. 133.
- Clinical Applications of ACTH and Cortisone. D. Goldring.—p. 136.

California Medicine, San Francisco

75:385-442 (Dec.) 1951

- Diagnosis of Pulmonary Coccidioid Infections. C. E. Smith.—p. 385.
Recent Advances in Thoracic Surgery. H. C. Maier.—p. 392.
Study of Small Bowel Tumors with Special Emphasis on Clinical Aspects. E. J. Joergenson and L. A. Weibel.—p. 395.
The Physician and the Atomic Bomb. V. P. Bond, M. C. Fishler and W. H. Sullivan.—p. 400.
Rh Factor in Rural Practice: Responsibility of the General Practitioner. J. L. Dennis.—p. 408.
Insulin and Insulin Mixtures—NPH Insulin. D. K. Burnham.—p. 412.
Effectiveness of Smear Technique in Detection of Pulmonary and Gastric Cancer. H. S. Aijian and B. Browell.—p. 416.
Enuresis. D. A. Charnock.—p. 421.
Primary Postpartum Hemorrhage. G. F. Melody.—p. 425.

Cancer Research, Chicago

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- Conception of Tumor Autonomy Based on Transplantation Studies: Review. H. S. N. Greene.—p. 899.
Method of Transplanting Gastric Mucosa to Anterior Abdominal Wall of Rat for Local Application of Carcinogens. E. W. Toovey, L. Heller and D. R. Webster.—p. 912.
Choline Oxidase Activity in Rat Liver During 3'-Methyl-4-Dimethylaminoazobenzene Carcinogenesis. G. E. Woodward.—p. 918.
Experimental Inhibition of Carcinoma by Lymphosarcoma. A. Bruwer, T. C. Donald Jr., G. M. Higgins and others.—p. 922.
Catalase Studies on Protein-Depleted Rats Bearing Jensen Sarcoma. D. Appleman, E. R. Skavinski and A. M. Stein.—p. 926.
Nature of Antigen in Induced Resistance to Tumors. M. K. Barrett, W. H. Hansen and B. F. Spilman.—p. 930.
Effect of High Levels of Certain Steroids on Induced Lymphocytic Leukemia in Rat. T. C. Donald Jr. and G. M. Higgins.—p. 937.
Organ Erythrocyte and Plasma Volumes of Tumor-Bearing Mice: Oligemia of Neoplasms. R. H. Storey, L. Wish and J. Furth.—p. 943.
Tocopherol in Tumor Tissues and Effects of Tocopherol on Development of Liver Tumors. R. W. Swick and C. A. Baumann.—p. 948.
Differences in Adrenal Responsiveness to Post-Castrational Alteration as Evidenced by Transplanted Adrenal Tissue. R. A. Huseby and J. J. Bittner.—p. 954.

Delaware State Medical Journal, Wilmington

23:323-352 (Nov.) 1951

- Office Management of Diabetes. P. S. MacNeal.—p. 323.
Psychiatric Consultations in General Hospital. S. G. Rogg.—p. 339.
Endocrinology in Gynecological Practice. R. C. Hayden.—p. 342.
Tracheotomy in Poliomyelitis. G. J. Boines.—p. 345.
Tuberculosis Today. G. T. Evans.—p. 347.

Diseases of Chest, Chicago

20:575-692 (Dec.) 1951

- Intravenous ACTH Therapy in Treatment of Bronchial Asthma. M. S. Segal and J. A. Herschfus.—p. 575.
Coccidioidomycosis: Review. H. G. Trimble.—p. 588.
Double Aortic Arch (with Report of Case with Rare Type of Functioning Double Arch Consisting of Slightly Larger Anterior Right Arch, Smaller Posterior Left Arch, Right Descending Aorta and Left Ligamentum Arteriosum). C. F. Storey and J. W. Crittenden.—p. 611.
Acute Pulmonary Oedema, Endogenous and Exogenous Causes, with Therapy. E. L. Belknap.—p. 630.
Pneumectomy in Treatment of Tuberculosis in Children. G. M. Botelho, A. Chapchap, H. L. G. Pereira and O. V. Cordeiro.—p. 642.
Late Complications of Extrapleural Pneumonolysis with Plombage. J. Goorwitch.—p. 651.
Local Thiostemicarbazone Therapy in Tuberculous Empyema. M. R. Lichtenstein.—p. 668.
Antibacterial Action of Citrus Peel Oil on Tubercle Bacillus in Vitro. B. L. Brock and H. M. Ketchum.—p. 671.

Intravenous Administration of Corticotropin in Bronchial Asthma.—Ten patients with severe, acute, or intractable bronchial asthma were given corticotropin (ACTH) intravenously. The patients were given a continuous infusion of 5% dextrose in distilled water (3 liters every 24 hours) containing 0.5 gm. of aminophylline to which 10 mg. of corticotropin per liter was added. A total of 30 mg. of corticotropin every 24 hours was given for one or more days. As improvement occurred, the dose was decreased to 15 or 10 mg. per 24 hours until recovery was obtained. Treatment was continued for one to nine days, the total dose ranging from 10 to 210 mg. of corticotropin, i. e., one-fifth to one-eighth of that required intramuscularly. Subjective clinical improvement with a sense of euphoria was noted rapidly. Remissions for as long as six weeks were obtained in

seven patients, while partial remissions were observed in the others. There were no therapeutic failures. During the follow-up period (1 to 10 weeks) two severe recurrences were observed 3 and 8 weeks, respectively, after treatment. Intravenous administration of corticotropin was particularly effective in one patient who had exhibited eosinophil escape and resistance to intramuscularly administered corticotropin. There were no allergic reactions to the drug, although high temperature of unknown origin occurred in two patients. Large doses of aminophylline and antibiotics were administered orally and rectally following discontinuation of corticotropin to prolong the remissive state.

Gastroenterology, Baltimore

19:383-598 (Nov.) 1951

- Roentgen Findings in Ileo-Jejunitis. R. H. Marshak, A. I. Friedman, B. Wolf and B. B. Crohn.—p. 383.
*Appraisal of Long-Term Results of Surgical Treatment of Regional Ileitis. J. H. Garlock, B. B. Crohn, S. H. Klein and H. Yarnis.—p. 414.
Diagnosis of Hepatitis. V. M. Sborov and T. C. Kesser.—p. 424.
Liver in Sarcoidosis. H. Shay, J. E. Berk, M. Sones and others.—p. 441.
Morphologic Consequences of Acute Exogenous (Staphylococcal) Gastroenteritis on Gastric Mucosa. E. D. Palmer.—p. 462.
Skin Lesions in Association with Ulcerative Colitis. M. H. Samitz and M. S. Greenberg.—p. 476.
Motility of Pelvic Colon and Rectum of Normal Persons and Patients with Ulcerative Colitis. E. A. Spriggs, C. F. Code, J. A. Bargen and others.—p. 480.
Motility of Distal Colon in Nonspecific Ulcerative Colitis. F. Kern Jr., T. P. Almy, F. K. Abbot and M. D. Bogdanoff.—p. 492.
Wernicke's Disease: Clinical and Pathological Study of 9 Cases. R. S. Boles and R. S. Boles Jr.—p. 504.
Observations on Effect of Drugs upon Intestinal Intubation. M. O. Cantor and H. P. McGinness.—p. 516.
Evaluation of Secretin Test in Pancreatic Disease. E. W. Heffernon and A. R. Gunter.—p. 526.
Effects of Complete Vagotomy on Pyloric Sphincter and Gastric Evacuation Mechanism. J. P. Quigley and H. Louckes.—p. 533.
Erythrocyte and Serum Cholinesterase in Ulcerative Colitis. H. C. Moeller, J. A. Rider and J. B. Kirsner.—p. 538.
Effect of Adrenocorticotrophic Hormone upon Fecal Lysozyme Titer in Ulcerative Colitis. R. W. Reifstein and S. J. Gray.—p. 547.
Correction of Steatorrhea in Bile Fistula Dogs by Duodenal and Oral Administration of Bile Substitutes. G. W. Searle and J. H. Annegers.—p. 558.
Effect of Various Compounds on Trypsin Activity. J. C. Calandra, L. L. Hardt and E. S. Stanish.—p. 564.

Surgical Treatment of Regional Ileitis.—The authors had previously reported on 137 patients operated on for regional ileitis or ileocolitis and followed for from 2 to 14 years. In this report the period of observation of 126 had lengthened to 9 to 21 years. The recurrence rate rises slowly the longer patients operated on for regional ileitis are followed, but it is pointed out that there is a long period of excellent health before recurrence if operative treatment is considered palliative rather than curative. No other form of therapy is as beneficial for so long a period. There appears to be a pronounced difference in the mortality and recurrence rates of patients subjected to ileocolostomy and of those subjected to ileocolic resection. In the former there were no operative deaths, and the over-all recurrence rate was 22.8%. In the latter the mortality was 14% and the over-all recurrence up to 46%. Late recurrences tended to heal spontaneously. It would seem as if the original virulence of the disease had "burnt itself out." Eight patients died years later of intestinal obstruction due to mechanical causes, but the authors do not believe that the incidence of late obstruction in this particular group is any greater than would be found in all patients who have undergone abdominal operations. Recent experience with extensive resections of the small bowel for jejunoileitis in a few additional patients demonstrated their rapid recovery, weight gain, and minimal bowel disturbance. For many years surgeons believed that extensive resections for diffuse small bowel disease would necessarily result in severe nutritional disturbances frequently incompatible with life. In one patient referred to above, only 3½ ft. (107 cm.) of normal jejunum remained. Yet there was a weight gain of 30 lbs. (13.6 kg.), diarrhea was minimal, and the patient returned to work. This change in attitude toward radical and extensive small bowel resection may alter the approach to the recurrence problem in surgical treatment of ileitis.

GP (J. Am. Acad. Gen. Practice), Kansas City, Mo.

4:1-210 (Dec.) 1951

- Misconceptions About Uterine Cancer. R. B. Scott and J. W. Reagan.—p. 35.
 Confident Childbirth. E. M. Marsh.—p. 43.
 Examination of Apparently Well Baby. K. Hammond.—p. 53.
 Acute Head Injuries. H. J. Svien and H. W. Dodge Jr.—p. 59.
 Analyzing Psychosomatic Relationships. I. Stevenson.—p. 67.
 Practical Therapeutics—Treatment of Bronchial Asthma. A. H. Unger and L. Unger.—p. 79.

Illinois Medical Journal, Chicago

100:325-378 (Dec.) 1951

- Physiography and Disease in Illinois. D. J. Davis.—p. 326.
 Management of Deafness. G. E. Shambaugh Jr.—p. 335.
 Complications of Puerperium. C. G. Collins, J. H. Collins and F. G. Nix.—p. 338.
 The Practicing Physician and Public Health. W. L. Biering.—p. 344.
 Some Observations on Gastro-Intestinal Distention. W. G. Maddock.—p. 349.
 Has Sympathectomy Kept Its Promise in the Treatment of Essential Hypertension? G. de Takals.—p. 353.
 Ambulatory Treatment of Retinal Vascular Disease. F. W. Parker.—p. 358.
 Subdeltoïd Bursitis. H. O. Hallstrand.—p. 361.
 Short Study of Iritis: Significance of Early Diagnosis and Treatment. J. Shanks.—p. 366.

International Journal of Leprosy, New Orleans

19:265-394 (July-Sept.) 1951

- Sulfoxone Sodium (Diasone) in Treatment of Leprosy: Summary Analysis of Field Reports. E. R. Kellersberger and W. Rule.—p. 265.
 Leprosy and Antileprosy Activities in Indonesia. R. Boenjamin.—p. 277.
 Leprosy in Prisons of French Guiana; Its Evolution During Century (1852-1950): Particulars. H. Floch.—p. 283.
 Pathogenesis of Bone Changes in Neural Leprosy. J. Barnetson.—p. 297.
 *Contribution to Study of Serology of Leprosy. N. Olmos Castro and A. A. Bonatti.—p. 309.
 Colloidal Gold Reaction in Spinal Fluid in Leprosy. R. P. Koenigstein and S. T. Chang.—p. 323.

Serology of Leprosy.—Since 1943 Olmos Castro and Bonatti have investigated specific changes in the serum in leprosy. They employed a lipid extract of leproma tissues as the antigen of microflocculation and complement fixation tests. The microflocculation test is preferred because of its simplicity. Two techniques have been used, the qualitative or diagnostic reaction and the quantitative or dosimetric reaction. The quantitative technique is employed for interpretation of the clinical form and stage of the infection. The authors discuss the pathogenesis of the serologic phenomena and show that the microreaction is of the specific heterophilic type. Serologic tests may be useful in determining whether conditional paroles should be granted to patients with nodular leprosy.

Journal of Allergy, St. Louis

22:487-586 (Nov.) 1951

- Purpura Due to Food Sensitivity: The Use of Skin Testing in Etiological Diagnosis. G. R. Ancona, M. J. Ellenhorn and E. H. Falconer.—p. 487.
 Bronchial Asthma, Urticaria, and Allergic Rhinitis from Tannic Acid. T. G. Johnston, A. G. Cazort, H. N. Marvin and others.—p. 494.
 Significance of Antistreptolysin Titer in Respiratory Allergy. C. Y. Sugihara and T. L. Squier.—p. 500.
 Immunophysiology of Serum Sickness: Alterations in Blood Volume and Thiocyanate Space in Relation to Humoral Antibodies in Rabbits Sensitized with Human Albumin or Globulin. J. K. Aikawa, E. H. Yount, G. T. Harrell and T. M. Jennings.—p. 508.
 Topical Application of Cortisone in Intractable Bronchial Asthma. M. London and F. W. Alexander.—p. 518.
 Effect of Miami (Fla.) Climate on Imported Allergic Problems. N. Zivitz.—p. 524.
 Pollen Counts: Variability and Percentage Error in a Given Location Under Standard Conditions. J. Spiegelman and G. I. Blumstein.—p. 536.
 Comparative Skin Testing in Antecubital and Popliteal Spaces. R. D. Wiseman.—p. 541.
 Purpura Simplex Due to Antihistaminic Drugs. I. H. Uvitsky.—p. 544.
 Subcutaneous Emphysema in Bronchial Asthma. N. Van Wezel.—p. 547.
 Importance of Hyperplastic Sinusitis in Bacterial Allergy. R. C. Grove.—p. 550.

Journal of Clinical Investigation, Cincinnati

30:1157-1304 (Nov.) 1951

- Observations on Alterations in Electrolytes and Fluid Balance in Patients with Cirrhosis of Liver With and Without Ascites. W. E. Ricketts, L. Eichelberger and J. B. Kirsner.—p. 1157.
 *Systemic Toxic Responses of Patients to Treatment with Streptokinase Streptodornase (SK-SD). W. N. Hubbard Jr.—p. 1171.
 Mechanics of Airflow in Health and in Emphysema. H. Dayman.—p. 1175.
 Studies in Diurnal Variation of Water and Electrolyte Excretion: Nocturnal Diuresis of Water and Sodium in Congestive Cardiac Failure and Cirrhosis of Liver. R. Goldman.—p. 1191.
 Renal Function as Factor in Fluid Retention in Patients with Cirrhosis of Liver. S. H. Leslie, B. Johnston and E. P. Ralli.—p. 1200.
 *Urinary and Fecal Excretion of Mercury in Man Following Administration of Mercurial Diuretics. J. Grossman, R. E. Weston, R. A. Lehman and others.—p. 1208.
 Renal Extraction and Excretion of Mercury in Man Following Intravenously Administered Mercurial Diuretics. R. E. Weston, J. Grossman, R. A. Lehman and others.—p. 1221.
 Turnover Rate of Serum Albumin in Man as Measured by ¹²⁵I-Tagged Albumin. K. Sterling.—p. 1228.
 Serum Albumin Turnover in Laennec's Cirrhosis as Measured by ¹²⁵I-Tagged Albumin. K. Sterling.—p. 1238.
 Circulatory Effects of Raised Airway Pressure During Cyclopropane Anesthesia in Man. H. L. Price, B. D. King, J. D. Elder and others.—p. 1243.
 Interrelationships of Cardiovascular, Renal and Electrolyte Effects of Intravenous Digoxin in Congestive Heart Failure. L. W. Eichna, S. J. Farber, A. R. Berger and others.—p. 1250.
 Effect of Mercurial Diuretics on Renal Ammonia and Titratable Acidity Production in Acidotic Human Subjects with Reference to Site of Diuretic Action. R. E. Weston, J. Grossman and L. Leiter.—p. 1262.
 Studies with Inagglutinable Erythrocyte Counts: III. Kinetics of Erythrocyte Destruction in Human Beings. R. F. Sheets, C. D. Janney, H. E. Hamilton and E. L. DeGowin.—p. 1272.
 Studies in Edema: III. Effect of Pitressin on Renal Excretion of Water and Electrolytes in Patients With and Without Liver Disease. A. G. White, G. Rubin and L. Leiter.—p. 1287.
 Site of Inhibition of Blood Clotting by Soy Bean Trypsin Inhibitor. M. B. Glendening and E. W. Page.—p. 1298.

Toxic Responses to Streptokinase-Streptodornase.—Twenty-eight patients who received 90 local instillations of streptococcic concentrates containing streptokinase and streptodornase for a variety of suppurative and hemorrhagic diseases were observed for evidence of acute and delayed toxicity. Of the 28 patients, 20 had one or more reactions lasting from 12 to 48 hours. Of the total of 44 reactions, 22 consisted of fever associated with leukocytosis and appearance of formed elements in the urine, and sometimes with glycosuria and proteinuria. Fever appeared within 4 to 6 hours, reached its maximum level within 24 hours, and disappeared within 24 to 48 hours. The remaining 22 reactions were afebrile and consisted of an increase in white or red blood cells in the urine or of leukocytosis. The cause of the reactions has not yet been clearly determined, but they may be due primarily either to foreign materials present in the solutions of streptokinase-streptodornase or to the breakdown products of their enzymatic action. Delayed toxicity was not observed in any patient.

Urinary and Fecal Excretion of Mercury.—The 24 hour urinary and fecal excretions of mercury after repeated administration of mercurial diuretics were studied in 17 patients, 13 of whom were in congestive heart failure with a restricted daily sodium intake of 8 to 10 mEq. Following intravenous or subcutaneous injection of 2 ml. of mercaptomerin (thiomersin®) sodium or intramuscular injection of 2 ml. of meralluride injection (mercubhydrin®), about 60 to 95% of the injected mercury was excreted in the urine during the first 24 hours. Mercury continued to appear in the urine for the next day or so in highly variable amounts. Daily fecal excretion of mercury rarely exceeded 1 to 2 mg. for the days immediately following the injection, but measurable quantities (greater than 0.3 mg.) were recovered for some time thereafter. After intravenous injection of a mercurial diuretic approximately 50% of the mercury was excreted in the urine within two and a half to three hours. After subcutaneous injection the rate of mercury excretion during the first 30 to 60 minutes was reduced. In most cases it was impossible to recover all the mercury even when analyses were continued over a considerable period. Mercaptomerin sodium and meralluride injection do not appear to differ significantly with respect to the

fraction of the injected mercury that can be accounted for. Neither ammonium chloride, which enhances, nor desoxycorticosterone acetate, which inhibits, the diuretic response to mercurials affected the renal excretion of mercury. In one patient, aminophylline (theophylline ethylenediamine) administered simultaneously with a mercurial diuretic but into a separate vein produced an early pronounced increase in urinary mercury excretion. With respect to recently proposed regimens involving frequent, even daily, administration of mercurials, the authors' results suggest that daily administration of 2 ml. of a mercurial diuretic would inevitably lead to accumulation of mercury in the body. The early excretion of a large fraction of the injected mercury before the onset of diuresis supports the concept that relatively little of the administered mercurial is actively involved in the production of diuresis. More knowledge of the forms of excretion of mercury and their filterability is essential.

Journal of Infectious Diseases, Chicago

89:209-306 (Nov.-Dec.) 1951

- Experimental Human Salmonellosis: III. Pathogenicity of Strains of *Salmonella* Newport, *Salmonella* Derby, and *Salmonella* Bareilly Obtained from Spray-Dried Whole Egg. N. B. McCullough and C. W. Eisele.—p. 209.
- Pathogenicity of Mucoid Variants of *Brucellae* for Guinea Pigs. L. M. Jones and D. T. Berman.—p. 214.
- Effect of Pituitary Adrenocorticotrophic Hormone on Experimental Tetanus in Mice. S. Spector and R. D. Mercer.—p. 224.
- Recovery of L Forms of *Brucella* and Their Relation to *Brucella* Phage. E. L. Nelson and M. J. Pickett.—p. 226.
- Kinetic Aspects of Hemolysis by α -Toxin of *Clostridium Welchii* and Its Inhibition by Antitoxin. W. Burrows.—p. 233.
- Antigenic Differences in Two Tuberculin Protein Fractions. F. B. Seibert, C. Crumb and E. H. Dufour.—p. 252.
- *Experimental Human Salmonellosis: IV. Pathogenicity of Strains of *Salmonella* Pullorum Obtained from Spray-Dried Whole Egg. N. B. McCullough and C. W. Eisele.—p. 259.
- Growth and Manometric Studies on Carbohydrate Utilization of *Brucella*. N. B. McCullough and G. A. Beal.—p. 266.
- Studies in Pathology and Pathogenesis of Experimental Brucellosis: III. Investigations Pertaining to Function of Spleen. A. I. Braude and W. W. Spink.—p. 272.
- Studies on Mechanism of Antagonism by *Aerobacter* Strains. R. E. Bowling and E. S. Wynne.—p. 277.
- Studies in Bacillary Dysentery: III. Mobilization of Specific Antibody into Intestine of Rabbit as Response to Homologous Living Dysentery Bacilli. L. M. González and E. Koppisch.—p. 281.
- Studies on in Vivo Fate of *Brucella* Variants with Different Virulence. W. Braun, A. N. Gorelick, M. Kraft and D. D. Mead.—p. 286.
- Influence of Sex of Mice on Histamine Sensitivity and Protection Against *Hemophilus Pertussis*. M. Pittman.—p. 296.
- Comparison of Histamine-Sensitizing Property with Protective Activity of *Pertussis* Vaccines for Mice. M. Pittman.—p. 300.

Salmonellosis from Spray-Dried Whole Egg.—This is the fourth of a series of investigations on the pathogenicity for man of strains of *Salmonella* organisms obtained from spray-dried whole egg. In the earlier studies the pathogenicity of *Salmonella* meleagridis, *S. anatun*, *S. newport*, *S. derby*, and *S. bareilly* derived from spray-dried whole egg were reported. The present paper reports studies with *S. pullorum*. The volunteers were inmates of a state prison. On admission all inmates of this institution are routinely given prophylactic immunization against typhoid, and yearly booster shots are administered thereafter. Since most of the subjects were long term inmates, many had received this immunization repeatedly. Three strains of *Salmonella* pullorum from spray-dried whole egg and one strain from a human were fed to the volunteers in graduated dosages. Illness was produced with all four strains in dosages ranging from 1.3 to 10 billion organisms. The characteristic illness was fulminating but brief. The organism was isolated from the stool only on the first or second day of illness. The organism was never recovered when fed at levels lower than those producing illness. Brief clinical histories are given of 27 of the volunteers. The dosages of the strains derived from spray-dried egg were of the same order of magnitude as those required with the strain obtained from a human. Much larger doses of *S. pullorum* strains were required to produce illness than of the other *Salmonella* strains. The clinical picture produced by *S. pullorum* was somewhat different from that noted with the other species. The explosive onset of illness in a number of the subjects is noteworthy, as well as the acute nature of most of the illnesses. The high fever and prostration on the first day of illness was

striking. Although the illness was often fulminating, recovery was surprisingly prompt, most subjects recovering in two or three days. The authors speculate on the possible modifying effects of the previous typhoid immunization and the size of the infective dose on the nature of the illness.

Journal Nat. Cancer Inst., Washington, D. C.

12:1-258 (Aug.) 1951. Partial Index

- On Etiology of Some Human Cancers. J. Clemmesen.—p. 1.
- Function of Transplantable Tumors of Thyroid Gland in C3H Mice. S. H. Wollman, H. P. Morris and C. D. Green.—p. 27.
- Studies of Various Tests for Malignant Neoplastic Diseases: VI. Tests for Least Coagulable Serum Protein and Iodoacetate Index. L. D. Ellerbrook, E. C. Meek and S. W. Lippincott.—p. 49.
- Relation of Cortisone-Induced Lymphopenia to Transplanted Sarcoma in Hamsters. E. D. Crabb and M. A. Kelsall.—p. 91.
- Studies on Blood Supply of Tumors in Man: III. Vascular Patterns of Liver by Hepatic Arteriography in Vivo. H. R. Bierman, R. L. Byron Jr., K. H. Kelley and A. Grady.—p. 107.
- Blood Pentolysis in Rats Bearing Induced Sarcomas: Evaluation. S. N. Steen.—p. 195.
- Modification of Irradiation Injury in Mice and Guinea Pigs by Bone Marrow Injections. E. Lorenz, D. Uphoff, T. R. Reid and E. Shelton.—p. 197.

J. Neuropath. and Clinical Neurology, Chicago

1:261-326 (Oct.) 1951

- Sclerodermal Muscular Atrophy Associated with Fasciculations: Clinical-Pathological Study of a Case. G. B. Hassin and P. M. Levin.—p. 261.
- Clinically Unsuspected Carcinoma of Lung with Multiple Metastatic Lesions in Brain; Neurologic Findings Not Readily Explained by Location of Metastases in Brain: Report of Case. W. Riese and J. M. Meredith.—p. 278.
- Subacute Ascending Paralysis of Duchenne: Report of Two Cases. I. C. Sherman and R. L. Tentler.—p. 285.
- Impregnation of Oligodendroglia in Cobalt-Fixed and in Paraffin-Imbedded Material. R. C. Lewis.—p. 291.
- Ocular Palsies Associated with Diabetes Mellitus. L. A. Kaplan.—p. 295.
- Treatment of Sciatica (Including That Caused from Herniated Discs) by Presacral Injection of Novocaine. A. Stender.—p. 301.
- Seizure Manifestations Ipsilateral to Cerebral Lesion. F. M. Forster.—p. 309.
- Tumor in Neck Produced by Thorotrast Spilled into Tissues During Arteriography. R. K. Jones.—p. 313.
- Periodic Paralysis Associated with Hyperthyroidism: Case Report. R. D. Kepner.—p. 316.
- Nocturnal Dysesthesias: Schultze-Wartenberg Syndrome. G. B. Hassin.—p. 320.

Journal of Thoracic Surgery, St. Louis

22:439-548 (Nov.) 1951

- Prognosis of Residual Bronchiectasis After Incomplete Resection. G. P. Rosemond, W. E. Burnett and J. Humphrey-Long.—p. 439.
- Radical Pneumonectomy. W. G. Cahan, W. L. Watson and J. L. Pool.—p. 449.
- Pleuropulmonary Resection with Hemidiaphragmectomy: Preliminary Report. B. H. Cotton and J. R. F. Penido.—p. 474.
- Management of Patient with Inoperable Cancer of Chest. R. H. Meade Jr. and R. A. Rasmussen.—p. 490.
- *Radioactive Isotopes in Palliative Management of Carcinomatosis of Pleura. E. M. Kent and C. Moses.—p. 503.
- Identification of Regional Lymph Nodes in Treatment of Bronchiogenic Carcinoma. J. A. Weinberg.—p. 517.
- Temporary Unilateral Occlusion of Pulmonary Artery: New Method of Determining Separate Lung Function and of Radiologic Examinations. E. Carlsen, H. E. Hanson and B. Nordenström.—p. 527.
- Observations on Hemodynamics of Bronchialpulmonary Vascular Communications. D. P. Shedd, R. D. Alley and G. E. Lindskog.—p. 537.

Radioactive Isotopes in Carcinomatosis of Pleura.—Carcinomatosis of the pleura with profuse effusion is one of the complications of malignant neoplasms. Patients with this complication have recurring, severe dyspnea as the pleural space fills with fluid after each aspiration. Efforts to stop or delay the formation of pleural fluid have been of little avail. Roentgen therapy offered some benefit, but since the rays cannot be directed accurately at the pleural implantations, even this proved largely ineffective. Radioactive isotopes were considered as a possible source of irradiation therapy, inasmuch as these substances can be injected directly into the pleural effusion and irradiate all surfaces of the cavity. An arbitrary dosage of 10 mc. of I^{131} was chosen initially for this investigation, but this dosage was later increased to as much as 30 mc. The I^{131} was transferred to a hot, sterile screw

cap bottle of 50 to 100 ml. capacity. The pleural effusion was aspirated into the bottle containing I^{131} , and then reinjected into the pleural cavity. This fluid was aspirated and reinjected several times in an attempt to deliver all of the isotope into the pleural space. Radioactive iodine in weak basic sodium sulfite solution was initially used, and when radioactive colloidal gold (Au^{198}) and I^{131} tagged human albumin became available, these isotopes were used in a few patients. Tables summarize the data obtained in the study of 19 patients, 14 of whom had primary carcinoma in the lung, 4 in the breast, and 1 in the anterior abdominal wall. Three of the 19 patients died too soon after therapy to evaluate the results, and in 3 patients the formation of pleural fluid was retarded but not entirely checked. In 13 patients the formation of pleural fluid was completely checked. Since I^{131} rapidly disappeared from the pleural space, the beneficial response is difficult to explain. It seems unlikely that a beta ray dosage large enough to cause severe destruction of tumor cells was delivered. However, there can be no doubt that fluid production was retarded or stopped. Perhaps this can be accomplished with beta radiation dosage much smaller than that necessary to cause tissue destruction. Additional experimental work is in progress to determine the optimum radiation dosage and most suitable isotope for this type of therapy.

Journal of Urology, Baltimore

66:735-830 (Dec.) 1951

- Renal Tuberculosis with Addison's Disease. W. J. Engel, R. S. Graves and R. W. Schneider.—p. 735.
 Differential Diagnosis Between Renal Tumors and Cysts. W. L. Ainsworth and S. A. Vest.—p. 740.
 Malakoplakia of Bladder. D. R. Higbee and T. E. Kilfoyle.—p. 750.
 Prevention of Urinary Incontinence Following Radical Prostatectomy: Preliminary Report. E. F. Hock.—p. 753.
 Spontaneous Activity of Detrusor Muscle in Cat. E. H. Ingersoll and E. S. Hegre.—p. 758.
 Departure from the Bag Catheter in Prostatectomy. J. W. Headstream and H. N. Marvin.—p. 765.
 *Prostatic Smear and Its Clinical Usefulness. H. Peters.—p. 770.
 Genital Tuberculosis in the Male; Concept of Its Pathogenesis and Treatment. R. F. Jones.—p. 778.
 Multicentric Origin of Papillary Tumors of Urinary Tract. J. H. Kaplan, J. R. McDonald and G. J. Thompson.—p. 792.
 Fluid Balance in Urological Patient: Disturbances in Renal Regulation of Excretion of Water and Sodium Salts Following Decompression of Urinary Bladder. B. Wilson, D. D. Reisman and C. A. Moyer.—p. 805.
 Acute Intermittent Porphyria. W. M. Ivers.—p. 816.

Usefulness of Prostatic Smear.—Of 341 patients from whom prostatic smears were obtained and studied in the division of urology at the University of Rochester School of Medicine, 72 had carcinoma of the prostate. A cancerous prostate sheds cells into the prostatic secretion that can be recognized microscopically. The prostatic smears of 63 of these 72 patients contained malignant cells, 6 contained cells suggestive of malignant growth, and 3 showed no characteristic cells (false negative smears). One false positive smear was reported as containing malignant cells, but benign prostatic hypertrophy was demonstrated on microscopic examination. Of the 72 patients who were later proved to have carcinoma, 3 were not suspected of having the disease when first seen; in these patients the prostatic smear aided in establishing the diagnosis earlier than would have been possible if cytological examination had not been made. Of several patients with prostatic carcinoma who were given estrogen therapy and followed with prostatic smears taken at intervals, 18 were observed long enough to give a preliminary report on the usefulness of the prostatic smear in evaluating cancer therapy. Eleven patients responded well to hormone therapy. Their prostates decreased in size and the consistency changed from hard to soft. The smears of eight of these patients showed either characteristically degenerated cells or, if the period of observation had been long enough, disappearance of the malignant cells. The smears of three patients with a good clinical response to therapy continued to show unaltered malignant cells. In seven patients the clinical response to therapy was poor, and all smears obtained from these patients continued to show malignant cells. Despite the small number of patients, the author's observations suggest that changes in the structure of the prostatic secretion or the failure of these changes to occur may be used as an additional guide to therapy.

Kansas Medical Society Journal, Topeka

52:525-576 (Nov.) 1951

- Surital Sodium: I. Clinical Use. P. H. Lorhan, G. Guernsey and M. M. Devine.—p. 525.
 Id.: II. Comparison with Pentothal Sodium. P. H. Lorhan and M. M. Devine.—p. 528.
 Treatment of Attack of Bronchial Asthma. E. A. Brown.—p. 529.
 Appendicitis: Review of 579 Cases. D. L. Evans.—p. 535.

Maine Medical Association Journal, Portland

42:355-384 (Dec.) 1951

- Simmonds' Disease Following Irradiation of Pituitary Gland for Acromegaly: Case Report. L. O. Warren.—p. 355.
 ACTH and Cortisone in Treatment of Weber-Christian Disease: Case Report. D. W. Drew, A. A. Wasson and L. E. Morris Jr.—p. 357.
 Problems Encountered in the Newborn Child: Symposium. B. L. Shapiro, E. E. Brown, F. C. Emery and A. W. Fellows.—p. 360.
 Chloroquine in Treatment of Acute Amebic Abscess of Caecum: Case Report. G. J. Tobias and B. G. Anderson.—p. 367.

Minnesota Medicine, St. Paul

34:1045-1132 (Nov.) 1951

- Neoplasms of Bony Pelvis Producing the Sciatic Syndrome. E. C. Paulson.—p. 1069.
 Intestinal Obstruction Associated with Fibrocystic Disease of Pancreas: Report of Three Cases. J. D. Rogers, A. H. Baggenstoss, J. E. Musgrove and R. L. J. Kennedy.—p. 1075.
 Treatment of Congestive Heart Failure. J. F. Briggs.—p. 1082.
 New Developments in Use of Cortisone in Rheumatoid Arthritis. P. J. Bilka.—p. 1088.
 Early Use of ACTH in Severe Burn: Report of Case. H. de Kruij and N. H. Baker.—p. 1092.
 Routine Use of Tub Baths in Postpartum Perineal Care. J. E. Hodgson and L. A. Day.—p. 1094.
 *Prevention of Postanesthetic Nausea with Dimenhydrinate (Dramamine®). D. K. Millett and M. O. Henry.—p. 1096.

Dimenhydrinate to Prevent Postanesthetic Nausea.—Millett and Henry used dimenhydrinate (dramamine®) as part of the preanesthetic medication in 69 patients undergoing anesthesia for orthopedic procedures ranging from simple manipulations to major reconstructions. The dosage of dimenhydrinate was 50 mg. for children and 100 mg. for adults given orally 30 to 45 minutes before surgery. It may also be given rectally as a suspension in 20 cc. of isotonic sodium chloride solution. The only other preanesthetic medication was morphine, 1/6 grain (11 mg.), with scopolamine (or atropine), 1/150 grain (0.43 mg.), for an average adult. The anesthetic used was 2.5% thiopental (pentothal®) sodium with 4 units of curare per cubic centimeter given intravenously and supplemented with nitrous oxide. The anesthetic time varied from 5 minutes to 2 hours and 35 minutes. An exact record was kept of any postanesthetic nausea or vomiting, and the patient's ability to take food and fluids by mouth. Thirty-three patients undergoing similar orthopedic operations served as controls. Four of the 69 patients who had received dimenhydrinate complained of some nausea after operation but did not vomit. A child who had received ether for nearly two hours vomited once. Twenty-five of the 69 patients had been subjected to anesthesia before, and 16 of these 25 recalled that they had had nausea and vomiting on the previous occasion. After having received dimenhydrinate, only 2 of the 25 were slightly nauseated. The authors observed no untoward reactions from dimenhydrinate, and they feel that it is a valuable addition to preanesthetic medication.

New Jersey Medical Society Journal, Trenton

48:537-584 (Dec.) 1951

- Abnormal Potassium Metabolism. R. D. Goodman II.—p. 539.
 Spontaneous Hematoma of Rectus Abdominus Muscle Simulating Acute Appendicitis. G. G. Carp.—p. 544.
 Quintuplet Pregnancy. A. C. Lawrence and A. J. Pauli.—p. 547.
 Psychiatric Problems in General Practice. A. Bronner.—p. 551.
 Nursery Procedure at the Englewood Hospital. G. Heller.—p. 554.
 Consecutive Myocardial Infarctions: Report of Three Attacks in a Young Man with Complete Recovery. B. B. Kun and T. J. White.—p. 556.
 "Functional Constipation": Case History. G. J. Kempe.—p. 562.
 Death from Anaesthesia. The Maternal Welfare Committee.—p. 563.

Physiological Reviews, Baltimore

31:345-512 (Oct.) 1951

- Metabolism of Hemin Chromoproteins. D. L. Drabkin.—p. 345.
 Micromethods and Their Application in Study of Enzyme Distribution in Tissues and Cells. H. Holter and K. Linderström-Lang.—p. 432.
 Carbohydrate and Fat as Factors in Protein Utilization and Metabolism. H. N. Munro.—p. 449.
 Structure and Physiological Functions of Ferritin. S. Granick.—p. 489.

Postgraduate Medicine, Minneapolis

10:459-538 (Dec.) 1951

- Fat Metabolism in Coronary Atheroma. M. B. Plotz.—p. 459.
 Malignant Ovarian Tumors. F. H. Falls.—p. 465.
 Surgical Treatment of Duodenal, Gastric and Anastomotic Ulcer. I. R. Trimble and D. H. Lynn.—p. 469.
 Gastric Vagotomy in Treatment of Peptic Ulcer. L. R. Dragstedt.—p. 482.
 Medical Responsibility for Juvenile Delinquency. N. Blackman.—p. 499.

Radiology, Syracuse, N. Y.

57:629-796 (Nov.) 1951

- Pulmonary Complications of Acute Bulbar Poliomyelitis. G. Jacobson, S. R. Cohen and R. A. Carter.—p. 629.
 Reticulo-Endotheliosis (Hand-Schüller-Christian Disease). J. R. Hodgson, R. L. J. Kennedy and J. D. Camp.—p. 642.
 Reticulo-Endotheliosis of Children: Treatment with Roentgen Rays. D. S. Childs and R. L. J. Kennedy.—p. 653.
 Pelvic Dimensions in Eutocia and Dystocia. P. C. Hodges and R. L. Nichols.—p. 661.
 Hepatolienography: Past, Present, and Future. S. F. Thomas, G. W. Henry and H. S. Kaplan.—p. 669.
 Roentgen Demonstration of Venous Circulation in Liver: Portal Venography. G. E. Moore and R. B. Bridenbaugh.—p. 685.
 Portal Venography: Preliminary Report. C. G. Child III, W. D. O'Sullivan, M. A. Payne and R. D. McClure Jr.—p. 691.
 Treatment of Radiation Sickness with ACTH: Preliminary Report of 14 Cases. K. W. Taber.—p. 702.
 Backache and Its Relation to Ruptures of Intravertebral Disks. K. Lindblom.—p. 710.
 Studies with Radioiodine: III. Problem of Dosage in Treatment of Hyperthyroidism. E. R. Miller and G. E. Sheline.—p. 720.
 Thyroid Carcinoma with Multiple Metastases and Pathological Fracture, Successfully Treated with Radioiodine: Report of Case. J. Sorrentino, B. Roswit and R. Yalow.—p. 729.
 Congenital Obstruction of Transverse Colon. N. Safran and A. M. Greenberg.—p. 738.
 Use of Nine and One-Half-Inch Roll-Film Cassette with Conventional Spot-Filming Fluoroscopic Tables for Angiocardiography. J. H. Wentworth.—p. 741.
 Preliminary Report on Radiography in Rapid Sequence. S. M. Wyman and F. Scholz.—p. 748.

Roentgen Treatment in Reticuloendotheliosis.—Reticuloendotheliosis is characterized by collections of hyperplastic reticuloendothelial cells in bone and soft tissue. Clinical and pathologic manifestations of this disease may vary, but three general types are recognized: Letterer-Siwe disease, Hand-Schüller-Christian disease, and eosinophilic granuloma of bone. This paper reports the experience at the Mayo Clinic with irradiation therapy in 12 children with reticuloendotheliosis. The first of these patients, who was seen in 1927, was treated with radium intermittently for a year. Fifteen years following the last treatment, the patient was apparently free from disease. The remainder of the patients received roentgen therapy. They were seen at intervals of from one to three months, and every active lesion was treated. For superficial lesions of the soft tissue and for lesions of the skull, mandible, or long bones, a single portal over the affected region was used. For more deeply situated lesions, such as those of the pelvic bones, liver, spleen, or lungs, treatment was given through several portals. A single dose of from 150 to 200 r, measured in air, was given at each portal. From one to four portals were used daily. The technical factors were 130 kv., half-value-layer 0.3 mm. Cu, distance 40 cm. The estimated tumor dose per lesion per course of treatment was approximately 200 r. All of the patients were four years of age or younger. Defects of the skull were present in every case; lesions of other bones were present in all but one. Six of the patients had lymphadenopathy, hepatomegaly, or splenomegaly. In only two cases was the entire triad of diabetes insipidus, exophthalmos, and bone defects observed. Nine of the 12 patients responded well to treatment and the disease seems arrested. In the other three patients the condition progressed rapidly and death ensued. The authors feel that radiation therapy should be tried in all cases of reticuloendotheliosis.

Corticotropin in Radiation Sickness.—Only patients who were treated exclusively with corticotropin (ACTH) after other methods of treatment had been discontinued and who have completed their radiation therapy have been selected for this report. Most of them had received intensive x-ray therapy for several weeks before becoming ill enough to warrant the corticotropin treatment. All were treated over the torso. Most of them were given 200 r (in air) of hard x-rays (half value layer 4 mm. Cu) daily or thrice weekly through sizable ports (approximately 10 by 15 cm.) totaling 2,000 r per port (in air). Fourteen patients were given 10 mg. doses of corticotropin intramuscularly, daily or thrice weekly while irradiation was continued. Twelve were relieved promptly after a few such injections. In one of these, several relapses occurred, but relief was obtained each time by a few more injections. In the 13th patient response was delayed, possibly due to renal complications incident to the primary disease. The 14th patient died of his primary disease during this study. White mice receiving 300 r of total body roentgen irradiation were kept alive by daily injections of corticotropin for 10 days in doses comparable to those given the human beings. Corticotropin also prolonged the lives of mice that received 600 r of total body irradiation, but it did not benefit those receiving larger doses. The results of the study to date indicate that corticotropin in small doses promptly relieves the symptoms of radiation sickness.

Radioiodine for Thyroid Carcinoma with Metastases.—A patient with papillary follicular adenocarcinoma of the thyroid gland with multiple bony and soft tissue metastases was treated with 1,246 mc. of radioactive iodine (I^{131}) over a period of more than two years. This patient has been clinically well for two years. His improvement began two months after institution of radioiodine therapy. A pathological fracture of the spine of the left scapula healed under radioiodine therapy and has remained healed to date. The growth potential of the metastatic lesions appears to have been arrested. Histologic changes due to irradiation have been demonstrated in the metastatic foci. Minimal changes have been demonstrated in the hemopoietic system, as well as a mild degree of renal tubular damage.

Review of Gastroenterology, New York

18:761-832 (Nov.) 1951

- Evaluation of End Results in Surgical Management of Chronic Duodenal Ulcers for Past 20 Years. J. W. Hinton.—p. 769.
 Allergy of Gastrointestinal Tract. A. F. R. Andresen.—p. 779.
 Newer Trends and Techniques in Gastroscopy. L. H. Berry.—p. 791.
 Sources of Error in Radiological Diagnosis of Gastrointestinal Tract Disease. J. S. Lehman.—p. 796.
 Treatment of Amebiasis. I. Snapper.—p. 801.
 Hemorrhoids: Etiology, Pathology and Treatment (Part I). R. V. Gorsch.—p. 806.

Rhode Island Medical Journal, Providence

34:569-624 (Nov.) 1951

- Common Conditions of Feet Often Confused with Fungus Infection. M. A. Winkler.—p. 585.
 Physical Examination in Industry as Cancer Case-Finding Procedure. C. D. Selby.—p. 588.
 Conclusions from 10 Years Investigation of Case Work Among Dermatitis Patients. F. J. Bailey.—p. 591.
 How Should Medical Records Librarian Meet Needs of Hospital?—Medical Records Librarian's View. E. L. Seymour.—p. 595.

Tennessee State Medical Assn. Journal, Nashville

44:493-536 (Dec.) 1951

- Problems in Treatment of Common Contagious Diseases. R. B. Lawson.—p. 493.
 Some Aspects of Clinical Electroencephalography. J. W. Ward.—p. 497.
 Carcinoma Arising in Fistula-in-Ano. C. H. Long.—p. 502.

West Virginia Medical Journal, Charleston

47:377-414 (Dec.) 1951

- Infections of Genito-Urinary Tract. J. A. C. Colston.—p. 377.
 Acquired Hemolytic Anemia (Case Report). C. H. Hiles.—p. 383.
 Play Therapy in Pediatric Maladjustment. A. S. Webster and C. G. Polan.—p. 387.
 Cutaneous Manifestations of Lymphoblastoma. J. Davis.—p. 390.
 Searching for the Truth About Things. Mrs. J. F. McCuskey.—p. 393.

FOREIGN

Annales Paediatrici, Basel

177:329-388 (Dec.) 1951

- *Generalized Eosinophilic Granuloma. W. Kintzen and R. Weber.—p. 329.
Gargoylism: Report of a Case. H. Jelke.—p. 355.
Nonsyphilitic Osteochondritis. F. Gerlőczy and K. Gefferth.—p. 374.

Generalized Eosinophilic Granuloma.—Two fatal cases of generalized eosinophilic granuloma are reported in a male infant aged three and a half months and in a man aged 40. Necropsy revealed generalized eosinophilic granuloma of the cervical, bronchial, axillary, retroperitoneal and inguinal lymph nodes, thymus, spleen, skeleton, lung, and pancreas in the infant, and generalized eosinophilic granuloma of the bone marrow, lymph nodes, and testes in the adult. Microscopic examination of the adrenal cortex revealed atrophy of the zona glomerulosa in the adult, while the adrenal cortex was unimpaired in the infant. Hyperpigmentation of the skin was observed only in the adult. The role of the adrenal cortex in eosinophilic granuloma is uncertain. The pathological observations in the authors' two cases showed that death may result from generalized eosinophilic granuloma in the absence of lesions of Letterer-Siwe disease (reticulosis) or Schüller-Christian disease (lipogranulomatosis).

British Journal of Cancer, London

5:289-374 (Sept.) 1951. Partial Index

- Histology of Adamantinoma. R. B. Lucas and A. C. Thackray.—p. 289.
Studies in Experimental Goitre: Malignant Change in Transplantable Rat Thyroid Tumour. H. D. Purves, W. E. Griesbach and T. H. Kennedy.—p. 301.
Induction of Tumors of Bladder Epithelium in Mice by Direct Application of Carcinogen. J. W. Jull.—p. 328.
Carcinogenesis in Parahibiotic Rats: Tumours of Ovary Induced by Acetylaminofluorene in Intact Females Joined to Gonadectomized Litter-Mates and Reaction of Their Pituitaries to Endogenous Oestrogens. F. Belschowsky and W. H. Hall.—p. 331.
Precancerous Changes Induced by 20-Methylcholanthrene in Mouse Prostates Grown in Vitro. I. Lasnitzki.—p. 345.
Basis for Selection of Carcinogens Likely to Produce Experimental Gastric Cancer. F. E. Ray and M. L. Jung.—p. 358.
Secretion by Stomach of Potential Carcinogens Derived from 2-Aminofluorene. F. E. Ray and J. H. Peters.—p. 364.

British Journal of Industrial Medicine, London

8:199-320 (Oct.) 1951. Partial Index

- Bearing of Experimental Psychology upon Human Skilled Performance. F. Bartlett.—p. 209.
Effects of BAL on Metabolism of Lead and on Symptomatology in Lead Intoxication. E. C. Vigliani and N. Zurlo.—p. 218.
Some Observations on Toxic Properties of 3:5-Dinitro-Ortho-Cresol. V. H. Parker, J. M. Barnes and F. A. Denz.—p. 226.
Value of Pulmonary Tomography in Investigation of Silicosis. L. Roche.—p. 236.
"Entente Radiologique." A Step Towards International Agreement on Classification of Radiographs in Pneumoconiosis. A. L. Cochrane, I. Davies and C. M. Fletcher.—p. 244.
*Pneumoconiosis in Boiler Scalars. H. E. Harding and A. P. Massie.—p. 256.
Hazards of Rope Making. J. A. Smiley.—p. 265.
Appliance for Prevention of Mercury Poisoning. F. Stocker.—p. 271.
Toxicologic Study of Trichloroethylene; Determination in Biologic Media. R. Farbe and R. Truhaut.—p. 275.
Toxicity of Methylal. F. L. Weaver Jr., A. R. Hough, B. Highman and L. T. Fairhall.—p. 279.
Effect of Benzene and of Carbon Tetrachloride on Concentration of Certain Vitamins, Fat, and Nitrogen in Liver of Rat. M. E. Shils, M. Sass, M. Wolke and others.—p. 284.
Plastic Splints and Appliances in Industrial Orthopaedics. J. T. Scales.—p. 288.
Environmental Study of Chromate Industry. M. Buckell and D. G. Harvey.—p. 298.
Carcinoma of Lung in Chromate Workers. P. L. Bidstrup.—p. 302.

Pneumoconiosis in Boiler Scalars.—Boiler scaling usually is done occasionally, but men who are engaged in this work full time run the risk of pneumoconiosis because the work is very dusty. Harding and Massie report on eight boiler scalars whose lungs they examined. The type of pneumoconiosis that commonly occurs in boiler scalars is similar to that found in coal workers. The deposition of dust is predominantly focal within small nodules distributed fairly evenly through the lungs, mainly in relation to perivascular, peribronchial, interlobular, and sub-

pleural lymphatics. In and around these deposits there is collagenous fibrosis that is usually not severe and commonly linear or radial. This type of reaction is often described as "dust reticulation," but the authors prefer the term "mixed dust fibrosis." Four of the eight patients had pneumoconiosis severe enough to produce disability and to be a factor in the cause of death. Two others had less extensive pneumoconiosis that probably was not a factor in their death. One of the remaining two patients had a minor degree of pneumoconiosis, and in the last one the pathological examination was inadequate. One of the eight patients had tuberculosis and two had bronchial carcinoma. Commenting on the fact that three died of bronchopneumonia, the authors state that others have observed a high incidence of upper respiratory infections in boiler scalars.

British Journal of Ophthalmology, London

35:637-750 (Nov.) 1951

- Clinical Value of Cortisone and ACTH in Ocular Disease: Preliminary Assessment for the Medical Research Council. S. Duke-Elder.—p. 637.
Series of Cases Treated Locally by Cortisone: Preliminary Report to Medical Research Council by the Panel on the Ophthalmological Applications of Cortisone and ACTH. S. Duke-Elder, O. M. Duthie, J. Foster and others.—p. 672.
Action of Cortisone on Tissue Reactions of Inflammation and Repair with Special Reference to the Eye. S. Duke-Elder and N. Ashton.—p. 695.
Effect of Cortisone on Healing of Corneal Wounds. N. Ashton and C. Cook.—p. 708.
Effect of Cortisone on Vascularization and Opacification of Cornea Induced by Alloxan. N. Ashton, C. Cook and M. Langham.—p. 718.
Effect of Cortisone upon Vascularization Which Follows Corneal Burns: I. Heat Burns. A. Lister and D. P. Greaves.—p. 725.
Effect of Cortisone on Permeability of Blood-Aqueous Barrier to Fluorescein. C. Cook and R. K. MacDonald.—p. 730.
Effect of Cortisone on Tissue Cultures. A. S. Steen.—p. 741.

British Journal of Radiology, London

24:581-636 (Nov.) 1951. Partial Index

- Influence of Radiology in Diagnosis and Treatment of Intrinsic Carcinoma of Larynx. S. Cade.—p. 582.
Percutaneous Vertebral Arteriography. D. Sutton and R. D. Hoare.—p. 589.
Radiographic Enlargements in Diagnostic Radiology. D. E. Fletcher and K. A. Rowley.—p. 598.
Wavelength of X Radiation at Depth in Water Irradiated by Beams of X Rays. J. R. Greening and C. W. Wilson.—p. 605.
Problems in Measurement of Bone Density. H. Jackson.—p. 613.
Protection of Mice Against Lethal Dose of X Rays by Cyanide, Azide and Malononitrile. Z. M. Bacq and A. Herve.—p. 617.

British Medical Journal, London

2:1359-1414 (Dec. 8) 1951

- What is the Job? L. Horder.—p. 1359.
*Treatment of Clinical Pneumonia with Antibiotics: Report by Subcommittee of Antibiotics Clinical Trials (Nontuberculous) Committee of Medical Research Council. J. G. Scadding and others.—p. 1361.
Aureomycin in Treatment of Pneumonia. M. B. Eadie, N. R. Grist and J. B. Landsman.—p. 1365.
Pneumonia in West London, 1949-1950. J. W. Crofton, J. W. Fawcett, D. G. James and others.—p. 1368.
Lung Involvement in Influenza. J. Fry.—p. 1374.
Effect of Cortisone on Reaction of Skin to Ultra-Violet Light. K. A. J. Järvinen.—p. 1377.
Observations on Temperature of Human Rectum. J. Grayson.—p. 1379.
New Example of Anti-S Agglutinin. J. J. van Loghem Jr., M. v. d. Hart and J. Cornelis.—p. 1383.

Treatment of Pneumonia with Antibiotics.—The introduction of aureomycin and chloramphenicol raised the question whether one of these might not be a better primary treatment for pneumonia than penicillin or the sulfonamides. A trial of aureomycin and chloramphenicol in clinical pneumonia was carried out by the Medical Research Committee of Britain at four centers—two in London, one in Sheffield, and one in Glasgow. Patients with diagnoses of pneumonia on admission were placed at random in one of three treatment groups: (1) those treated with aureomycin; (2) with chloramphenicol; and (3) by "standard treatment." Most of those in the last group were treated with penicillin, a few with sulfonamides. There were 267 cases in the series. The treatment groups were found to be comparable, and

the results of treatment were very similar in each group. Analysis of the cases in which patients were desperately ill on admission suggests that penicillin was at least as valuable as the other two antibiotics. Symptoms of drug toxicity were much commoner with aureomycin and chloramphenicol than with penicillin. Treatment with aureomycin was more than 10 times and with chloramphenicol more than 9 times as expensive as treatment with penicillin. In a choice between aureomycin, chloramphenicol, and penicillin, it was suggested that penicillin by injection is the best treatment for clinical pneumonia. In this recommendation no account is taken of the possible value of the sulfonamides, which were not compared with the other drugs in the present trial.

Clinica Pediatrica, Bologna

33:461-524 (Aug.) 1951. Partial Index

- *Effect of Aureomycin on Virus of Variola Vaccine. A. Degli Esposti.—p. 461.
- Rapid Recovery of Case of Kaposi's Varicelliform Disease Following Treatment with Aureomycin. L. Landucci.—p. 474.
- *Streptomycin Therapy in Typhoid Fever and Tuberculous Meningitis. P. Nicolaj.—p. 484.

Effect of Aureomycin on Virus of Variola Vaccine.—A 10-month-old child with a previous history of exudative diathesis had eczema vaccinatum with vesicular eruption on the face. The child was treated locally with a penicillin ointment in doses containing 75,000 Oxford units every six hours. The drug was also given parenterally. When on the eighth day of illness he was hospitalized, penicillin compresses were substituted for the ointment, and aureomycin therapy was begun. An initial dose of 250 mg. was followed by 125 mg. every six hours for four days. After a total dose of 2,250 mg. the patient was treated only locally with penicillin combined with 50 mg. of streptomycin every six hours for six additional days. The high temperature became intermittent and was normal after five days. Regression and desiccation of the vesicles followed a normal course. The patient was dismissed in good condition 23 days after onset of the disease. An effect of aureomycin in this case is doubted, since penicillin and sulfonamides had an equal effect in other patients with this illness. The author vaccinated eight children, 2 to 3 years old, who had had no prior vaccination. Two of these received orally 125 mg. and two 250 mg. of aureomycin every six hours for four days. The other four served as controls. Evolution of the reaction was the same in all eight children, although local responses were more pronounced in the controls. The author reports extensively on *in vitro* studies and on the morphological changes of the virus under great concentrations of aureomycin that he had observed with the electron microscope. He concludes, contrary to the American authors, that the drug has little effect on the virus of variola vaccine *in vivo* as well as *in vitro*. However, aureomycin is still today the most efficacious antibiotic drug for diseases due to this type of virus.

Streptomycin in Typhoid Fever and Tuberculous Meningitis.—Streptomycin intravenously in daily doses of 400 mg. and streptomycin intrathecally in doses of 35 mg. every three days were given to three children, 30, 21, and 11 months old, respectively, with tuberculous meningitis. The general condition of the patients improved, and the spinal fluid tended to normalization. In the first six months and in the second nine months after admission the temperature was elevated, and red spots appeared on the abdomen and thorax. Ten days later both had a positive Widal reaction. Chloramphenicol (chloromycetin®) was given orally in daily doses of 0.75 gm. for three days and subsequently in daily doses of 0.50 gm. and 0.25 gm. The first child recovered. Swelling of the right knee, indicating a localization of the *Eberthella bacillus*, occurred in the second patient to whom additional chloramphenicol and intravenous typhoid vaccine were administered. Ten days later temperature was normal and the patient well. These two patients recovered from typhoid without the tuberculous meningitis becoming worse. The third child had been cured of tuberculous meningitis and dismissed with sequelae of encephalitis. In this case the occurrence of typhoid fever caused severe anemia, spinal block, and aggravation of the encephalitic symptoms that resulted in death of the patient. The

assumption that the meningoencephalitis secondary to the typhoid disease was a relapse of the previous tuberculous meningitis was ruled out, and meningoencephalitis due to allergy or parallergy to chloramphenicol was suggested. In patients with prior history of encephalitic disturbance typhoid fever may reactivate the previous lesions and cause a toxic meningoencephalitis. But, as seen in the first two cases, typhoid fever does not always cause relapse of tuberculous meningitis.

Clinical Science, London

10:405-540 (Nov.) 1951

- Effect of Nephrectomy and Adrenalectomy upon Blood Pressure in Hypertensive and Normotensive Rats. M. A. Floyer.—p. 405.
- Nature of Hypertension Occurring in Nephrectomized Parabiologic Rat. J. M. Ledingham.—p. 423.
- Observations on Gross Pulmonary Fat Embolism in Man and Rabbit. J. Armin and R. T. Grant.—p. 441.
- Observations on Action of Parathyroid Hormone. M. D. Milne.—p. 471.
- Hyperfunction of Adrenal Cortex and Insulin Resistance in Diabetic Ketosis. J. M. Stowers.—p. 487.
- Oxygen Consumption of Polycythaemic Blood *In Vitro* with Note on Arterial Oxygen Saturation in Primary Polycythaemia. H. E. de Wardener and I. M. Young.—p. 497.
- Day-to-Day Changes in Sodium and Water Output With and Without Posterior Pituitary Extract. D. A. K. Black and A. E. Thomson.—p. 511.
- Changes of Pulse Pressure and Heart Rate Induced by Changes of Position in Subjects with Normal and Failing Hearts. P. Howard and G. L. Leathart.—p. 521.
- Circulatory Changes in Forearm Following Sympathectomy. R. S. Duff.—p. 529.

Deutsche medizinische Wochenschrift, Stuttgart

76:1485-1516 (Nov. 23) 1951. Partial Index

- Significance of Physiologic and Artificial Colloids for Regulation of Transport Functions in Animal Organism. H. Bennhold.—p. 1485.
- Possibilities and Limitations of Ophthalmoscopic Diagnosis of General Vascular Disease. W. Kyrieleis.—p. 1493.
- The Influenza Virus. G. Schramm.—p. 1496.
- Etiology and Prevention of Pulmonary Cancer. E. L. Wynder.—p. 1498.
- *Is the Reticulocytic Crisis in Treatment of Pernicious Anemia Dependent on Severity of Anemia? S. Sandkühler and E. Flak.—p. 1500.
- Late Success of Endometrial Transplantation. R. K. Kepp.—p. 1501.

Reticulocytic Crisis and Severity of Pernicious Anemia.—It is generally believed that the reticulocytic count in optimally treated pernicious anemia depends on the severity of the anemia, being higher in severer forms and vice versa. Some investigators even developed formulas to determine the numbers of the reticulocytes (proerythrocytes). Sandkühler and Flak point out that during relapse the level of reticulocytes is usually from 30,000 to 60,000 below the normal figure. With the onset of therapy they increase sharply and reach the maximum between the sixth and eighth day of treatment. They computed this maximum in absolute values on their own patients. Then they classified their cases according to the initial counts and compared these with the average values computed on the basis of the Riddle and of the Friedmann and Isaacs formulas. The table that lists these comparative figures reveals that neither the reticulocyte counts in their own cases, which they obtained by taking daily counts on 116 patients, nor those computed on the basis of the aforementioned two formulas were related to the initial erythrocyte count of the peripheral blood. They suggest that computation factors, particularly an overestimation of the relative auxiliary figures (expressed per thousand), might explain the formerly accepted relationship between initial erythrocytic figure and the maximum reticulocytic count. They argue that if there really were such a relationship it would have to take into consideration the bone marrow. The level of the reticulocytic count actually depends on the number of transformable megaloblasts in the bone marrow.

Edinburgh Medical Journal

58:521-564 (Nov.) 1951

- Osteoarthritis of Hip: Its Surgical Treatment. W. Mercer.—p. 521.
- Vascular Patterns in Cirrhotic Liver. J. B. Wilson.—p. 537.
- Iodine Therapy for Inadequate Lactation. R. A. Miller.—p. 548.
- Keloid and Self Administration of Adrenaline. C. K. Robertson.—p. 555.

Journal of Laryngology and Otology, London

65:749-808 (Nov.) 1951

- Irradiation of Nasopharynx in Eustachian Obstruction: Report of 48 Cases. J. C. Ballantyne.—p. 749.
 Fenestration Operation: Some Difficulties. W. McKenzie.—p. 756.
 Emergency Operations in Laryngo-Tracheal Dyspnoea. A. Réthi.—p. 773.
 Malignant Disease of Nasopharynx. F. C. Ormerod.—p. 778.

Journal of Physiology, London

115:123-248 (Oct.) 1951. Partial Index

- Methaemoglobin Formation in Dilute Solutions of Laked Erythrocytes and Its Inhibition by 'Stroma Factor.' G. Fegler.—p. 123.
 Plasma in Packed Cell Column of the Haematocrit. D. Leeson and E. B. Reeve.—p. 129.
 Fatigue of Mammalian Nerve in Relation to Cell Body and Vascular Supply. G. Causey and G. M. Schoepfle.—p. 143.
 Some Electrophysiological Observations on Isolated Single Myelinated Nerve Fibres (Saltatory Conduction). B. Frankenhaeuser and D. Schneider.—p. 177.
 Gastric Response to Pectin Meals of High Osmotic Pressure. J. N. Hunt, I. Macdonald and W. R. Spurrell.—p. 185.
 Intercellular Plasma and Its Effect on Absolute Red Cell Volume Determination. D. M. Jackson and M. E. Nutt.—p. 196.
 Hexamethonium and Insulin Hypoglycaemia. M. Schachter.—p. 206.

Lancet, London

2:1047-1096 (Dec. 8) 1951

- Selection of Medical Students. D. Brinton.—p. 1047.
 *Effect of Treatment on Renal Circulation in Heart-Failure. C. E. Davies.—p. 1052.
 Results of Hospital Treatment of Chronic Alcoholism. J. Harper and B. Hickson.—p. 1057.
 Antabus in Management of Chronic Alcoholism. J. N. P. Moore and M. O'C. Drury.—p. 1059.
 *Some Evidence Suggesting Suppression of Adrenocortical Function by Cortisone. H. W. McIntosh and C. B. Holmes.—p. 1061.
 Gastric Obstruction from Swallowing Corrosive Poison. M. Paul.—p. 1064.
 Non-Soapy Detergents and Prothrombin-Time Estimation. H. Lehmann.—p. 1066.

Treatment of Renal Circulation in Heart Failure.—In patients who recover from chronic cor pulmonale, renal function may apparently return to normal. In rheumatic heart disease, on the other hand, clinical improvement is not accompanied by kidney function. This paper reports observations before and after treatment on the glomerular filtration rate (inulin clearance), the effective renal plasma flow (*p*-aminohippuric acid clearance), and the capacity to excrete salt in patients with congestive heart failure due to chronic chest disease or chronic rheumatic heart disease. Two of seven patients with congestive heart failure due to rheumatic heart disease had not received digitalis before admission to hospital. In these two patients the acute effect of intravenous digoxin on the renal clearances and the rate of sodium excretion was observed, and the clearances were again measured after maintenance therapy with digitalis. The other five patients were given the same dose of digitalis they had received before admission to the hospital, and the effects on the renal circulation of protracted rest in bed, mercurial diuretics, and restriction of salt and of variations of the venous pressure were recorded. In patients with chronic cor pulmonale the effect of the following three forms of therapy were studied: (1) administration of pure oxygen for an hour; (2) intravenous administration of digoxin; and (3) protracted rest in bed and administration of mercurial diuretics and systemic penicillin. In patients from both groups the ability to excrete salt was tested after recovery from heart failure by observing the effect on body-weight and venous pressure of withholding diuretics and giving a diet containing 10 gm. of salt and 1500 ml. of fluid daily. The renal blood flow was reduced in both groups. Digoxin had no immediate effect on the renal circulation or on the rate of sodium excretion in either group. In patients with rheumatic heart disease, long continued treatment, leading to considerable clinical improvement, was not accompanied by any significant change in the renal circulation, and the ability to excrete salt remained severely impaired. Recovery from pulmonary heart failure, on the other hand, was accompanied by a considerable increase of renal blood flow and a small increase of glomerular filtration-rate, and the capacity to eliminate salt appeared to be restored to normal. Analysis of the factors involved in these different responses did not fully explain the mechanism, except that anoxia, venous congestion,

and pulmonary hypertension do not seem to initiate the disturbance of renal function. Hormonal factors may play a part, but the evidence is slight.

Suppression of Adrenocortical Function by Cortisone.—After citing clinical observations suggesting that the function of the adrenal cortex is suppressed when cortisone is given, and that this suppression is mediated through the pituitary, McIntosh and Holmes describe their own investigations on this problem. In men receiving long-continued cortisone treatment for rheumatoid spondylitis 17-ketosteroid excretion was decreased. This supports the hypothesis that adrenocortical function is depressed during cortisone therapy. Attention was next directed to the question of whether there is a decrease in the ability of the adrenal cortex to respond to a given stimulus, such as intramuscular injection of corticotropin. It was found that response to a single small injection of corticotropin during and after cortisone therapy is diminished. A response can be obtained in patients receiving cortisone following protracted stimulation with intravenous injections of corticotropin. Use has been made of the depression of adrenal activity by cortisone in the treatment of the adrenogenital syndrome resulting from adrenocortical hyperplasia. The effect of cortisone in treating Cushing's syndrome is under consideration. It has also been suggested that the response to cortisone may be used to distinguish between functionally active tumors and hyperplasia of the adrenal cortex. Functionally active tumors are not depressed by cortisone, being apparently independent of pituitary stimulation, whereas in hyperplastic lesions depression of activity can be demonstrated. The fact that adrenal cortical depression can exist after cessation of cortisone therapy should be recognized. Careful clinical handling of such patients may be necessary, especially if a surgical operation becomes necessary.

Revue de la Tuberculose, Paris

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- *Clinical and Bacteriologic Study of 58 Cases of Cavity Pulmonary Tuberculosis Treated with Streptomycin and Short Continuous Infusions of *p*-Aminosalicylic Acid. A. Duroux and P. J. Coletos.—p. 781.
 Effect of Cortisone on Tuberculous Allergy. E. Bernard and B. Kreis.—p. 802.
 Two Cases of Treatment with Cortisone and Corticotropin (ACTH) in Patients with Tuberculosis. F. Coste, Pierre-Bourgeois, P. Galmiche and Vic-Dupont.—p. 809.

Streptomycin and *p*-Aminosalicylic Acid in Pulmonary Tuberculosis.—Of 107 patients with cavitary pulmonary tuberculosis, 88 were treated with 1 gm. of streptomycin daily combined with an intravenous infusion of 500 cc. of a solution of 15 gm. of sodium *p*-aminosalicylate for two to three hours; 19 patients were given intravenous infusions of sodium *p*-aminosalicylate alone. Treatment was given for two to five months with a total dose of 60 to 200 gm. of streptomycin and 900 gm. to 3 kg. of sodium *p*-aminosalicylate. Some of the patients received 100 to 300 consecutive infusions without undesirable effects. In 18 patients venous sclerosis resulted from the infusions but treatment could be resumed after 10 to 15 day interruptions of the infusions. Erythema occurred in six patients, and rise of temperature after 30 to 40 infusions in five. Permanent discontinuation of the treatment was made necessary by shock with cardiovascular collapse in two patients. Gastrointestinal disturbances were exceptional as compared to those observed with oral treatment with *p*-aminosalicylic acid. Of the 88 patients, only 58 were followed up regularly for at least two months by bacteriological studies of resistance of tubercle bacilli to streptomycin and *p*-aminosalicylic acid. Results showed that except for three patients (5%) streptomycin resistance did not occur in the patients who were given streptomycin and *p*-aminosalicylic acid in combination. In four patients the combined treatment induced regression of a previous streptomycin resistance. The risk of *p*-aminosalicylic resistance proved to be negligible, even with the use of large doses of 1,500 to 3,000 gm. of the drug. Clinical and roentgenologic results obtained with infusion of *p*-aminosalicylic acid were definitely superior to those obtained with oral administration of the drug. All the undesirable effects observed with the infusion method were due to faulty technique of venous puncture.

BOOK REVIEWS

The Operation of Sickness Benefit Plans in Collective Bargaining. By Fred Slavick. Princeton University, Department of Economics and Social Institutions, Industrial Relations Section, Research Report Series no. 84. Paper. Pp. 109. Industrial Relations Section, Princeton University, Princeton, New Jersey, 1951.

Programs extending aid to workers during illness have sprung from the efforts of unions to advance the welfare of their members. Having thus placed sickness insurance in the framework of union organization, the author cautiously notes that sickness benefit plans create their own unique set of problems. Policy and administration, although related to the unions' broader operations, must develop through procedures best adapted to these plans. Organization and administration of benefit programs is the theme of this report that surveys 10 union-management plans established by collective bargaining. The present publication is an extension of an earlier study made in 1945 by the industrial relations section outlining the growth, provisions, and problems related to negotiated sickness insurance programs ("Group Health Insurance and Sickness Benefit Plans in Collective Bargaining"). Material from this earlier report, in addition to interviews and correspondence, are the sources for the present study.

Before outlining financial structure and administrative practices, the report summarizes the rapid rise of sickness benefit programs from their inception during World War II to 1950, when the Bureau of Labor Statistics reported agreements by nearly every major union in the country providing some form of benefit insurance; these benefits reached 7 million persons. World War II boosted insurance plans, and the wage stabilization program, which encouraged fringe benefits in lieu of increases in wage rates. During the postwar period, broadened welfare activities of trade unions and favorable decisions by the National Labor Relations Board placed sickness insurance within the province of collective bargaining.

Although the study indicates versatility in financial and administrative practices, recent trends, such as joint financing, extended membership coverage, increased protection to those insured, and standardization of benefits indicate an approach toward sounder, more widely accepted practices. Claim administration and financial operation of benefit plans under representative union-employer programs are discussed in some detail. Most of the programs in the report use a form of group insurance that is employer financed, carrier insured, and administered either by the union or by a union-employer arrangement. This generalization should not, however, obscure the fact that there are a variety of successful plans. Two chapters are devoted to an examination of the financial structure of each type of plan in order to discern the degree to which it meets five basic standards of financial operation.

With all their assets and defects, the plans have been considerably improved in this short period during which prevailing economic conditions have been favorable. Unions do not, however, regard present benefit plans as the only or the complete answer to the needs of their members for temporary disability benefits.

Recent legislation on temporary disability benefits, in several states, to the effect of standardizing such programs, has been influential in planning. A chart schematizing the 10 union programs studied is appended to the report. The study can best serve as a thorough introduction to sickness benefit plans in union-management negotiations.

The Healing Touch. By Harley Williams. Cloth. \$6.75. Pp. 370, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., 1951.

The author delineates a number of rare personalities who were important in their day. The book opens with portraits of three physicians to British royalty, two of whom served Queen Victoria. The royal physicians are Sir William Knighton, Sir James

Clark, and Sir William Jenner, who is not to be confused with Edward Jenner, the discoverer of vaccination. Their prerogatives as well as some of the difficulties in which they occasionally found themselves are mentioned, as are their efforts to save the life of Queen Victoria's husband, who died prematurely of typhoid. Incidentally, the age at which Prince Albert died is said to be 44 on page 73 of this book and 42 on page 105.

There are interesting pages on Sir Edwin Chadwick, whose father taught physics to John Dalton, the man who invented the atomic theory. William Worrall Mayo, "who emigrated to America where his later career had some of the characteristics of atomic energy itself" was a pupil of Dalton. Sir Edwin Chadwick had much to do with laying the foundation of modern sanitation and with establishing boards of health in England. Many pages are devoted to Florence Nightingale and to Charles Edouard Brown-Séquard. "Book Five—A New World of Medicine," the last part of the book, is given over largely to William and Charles Mayo of Rochester, Minnesota; and to William Henry Welch and William Stewart Halsted of Johns Hopkins University, whom the author calls respectively "Grand Lama of Johns Hopkins" and the "Recluse" as well as the greatest of the early American surgeons. Harvey Cushing is said to have been "one of those superior types whose intelligence continually overflows from the work they are doing." Aside from being a great surgeon, he collected first editions, wrote an outstanding biography of his friend, William Osler, and was brilliant at talking, tennis, and dancing. Many other outstanding medical personalities appear in this book in less detail. Intimate facts in the lives of these persons, along with interspersions of the author's own philosophy, make this book instructive and entertaining. Modern anatomists probably will differ with a statement on page 10 to the effect that anatomy was as far advanced in the 18th century as it is today.

The Specialties in General Practice. Edited by Russell L. Cecil, M.D. Cloth. \$14.50. Pp. 818, with 470 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1951.

In spite of ever-increasing medical specialization, the general practitioner is still the first physician to see most patients, and he is thereby called upon to make at least a tentative diagnosis and to either institute treatment himself or refer the patient elsewhere. Consequently, it is incumbent on him to keep abreast of developments in diagnosis and treatment in many fields, an impossible task if he must depend upon current literature or texts written by specialists for specialists. This book is designed to supply the general practitioner with authoritative information on recent diagnostic methods in diverse fields, to describe accepted treatments, and to indicate those conditions for which expert advice should be sought. Fourteen experts have each contributed a chapter on their specialties. The first three chapters are concerned with minor surgery, orthopedic surgery, and fractures. Subsequent chapters deal with urology, proctology, gynecology, obstetrics, pediatrics, ophthalmology, otolaryngology, dermatology, and psychiatry. In each chapter special methods of examination are described in detail, with many practical hints given. Emphasis is placed on diagnosis of the commoner conditions and recognition of the possible existence of relatively unusual diseases that require diagnostic steps not usually available in the general practitioner's office.

The selection of material for inclusion in such a book presents as insuperable a problem as that facing the editor of an anthology. No one will be completely satisfied, yet everyone will find some sections that are just what he has been looking for and has been unable to find elsewhere. The chapter on psychiatry, however, will be of distinct help to any physician who deals with patients. The book is well printed, with two columns on each page to facilitate reading. The illustrations are excellent, and the index is complete.

The 1951 Year Book of Obstetrics and Gynecology (August, 1950-June, 1951). Edited by J. P. Greenhill, B.S., M.D., F.A.C.S., Professor of Gynecology, Cook County Graduate School of Medicine, Chicago. Cloth. \$5. Pp. 567, with 134 illustrations. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1951.

This compact volume is a collection of abstracts of outstanding papers on obstetrics and gynecology that were published during 1951. Many of the abstracts are accompanied by concise and critical editorial comment, often with references to related papers, which provide orientation in the field. This feature enhances the value of the book, particularly for the nonspecialist.

In the first half of the volume, which is devoted to obstetrics, there are abstracts on such subjects as Richardson's biochemical test for pregnancy, roentgen pelvimetry, histological changes in the cervix during pregnancy resembling carcinoma in situ, and diagnosis and management of threatened abortion, ectopic pregnancy, toxemia, and coexisting disease during pregnancy. Papers evaluating the effect of different types of obstetric anesthesia on mother and infant are reviewed. The pathogenesis of congenital anomalies is considered in detail, as is the hyaline-like pulmonary membrane that frequently causes death in premature infants. In the gynecological section, there are abstracts dealing with hysterosalpingography, culdoscopy, infertility, genital tumors and infections, menstrual disorders, endometriosis, operative techniques, and hormone treatment of metastatic cancer of the breast. This volume can be recommended as a handy review and reference manual to all those who are interested in keeping up-to-date in this field.

Plastic Surgery of the Nose Including Reconstruction of War Injuries and of Deformities from Neoplastic, Traumatic, Radiation, Congenital, and Other Causes. By James Barrett Brown, M.D., Professor of Clinical Surgery, Washington University School of Medicine, St. Louis, and Frank McDowell, M.D., Assistant Professor of Clinical Surgery, Washington University School of Medicine. Cloth. \$10. Pp. 427, with 379 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1951.

This book is based on the personal experiences of the authors. Because of this, unnecessary theoretical discussion is omitted. The authors describe the operative procedures that they find to be the most practical and successful. Each operation is illustrated by two color step-by-step drawings. Photographs of patients show the results of treatment. The book is intended as a practical clinical work. Outmoded operations and more recent operations that the authors have found unessential are not included. This is advantageous and it avoids confusion. The basic teachings and techniques of Jacques Joseph of Berlin are fully discussed. Figure 7, page 23, shows this pioneer of corrective rhinoplastic surgery in the operating room. Before and after pictures are more convincing than verbal description. It is unfortunate that, in figure 93, page 114, the postoperative photograph does not show the patient smiling and the smile's effect on the lip as does the preoperative photograph. The book is written in a readable and refreshing style. The type is large and legible, and the material is inclusive. This outstanding work is recommended to all those interested in plastic surgery of the nose.

Methods in Medical Research. Volume 4. Maurice B. Visscher, Editor-in-Chief; Histochemical Staining Methods. George Gomori, editor; Fluid and Electrolyte Distribution, Louis B. Flexner, editor; Studies on Gastrointestinal Pressures, Innervation and Secretions, J. P. Quigley, editor; Tissue Culture Methods, C. M. Pomerat, editor. Cloth. \$7. Pp. 306, with illustrations. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1951.

This series of volumes is intended to provide ready accessibility of reliable detailed information on working methods to be used in research. The fourth volume is divided into four sections, each of which represents a major field in medical research. The first deals with histochemical staining methods for the presence of various inorganic elements and certain organic substances including the oxidative and hydrolytic enzymes. The second section concerns itself with fluid and electrolyte distribution. The methods for estimation of the volume of the body fluids as well as flame photometer techniques are described. The third division considers problems relative to digestive tract pressures, innervation, and secretions. The last section describes tissue culture techniques, including the media used and cytochemical studies. A copious bibliography accompanies each sec-

tion. The editors are to be congratulated, both for the concept and its execution in this volume. The text is solid, with little extraneous matter, and supplies much needed material on methodology as well as source material for additional information.

Forgotten Musicians. By Paul Nettl. Cloth. \$4.75. Pp. 352. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1951.

Music and medicine, the most universal of the arts, have much in common. Many physicians have found release and inspiration in the enjoyment of music, and, on occasion, physicians have been excellent musicians in their own right. Theodore Billroth, the father of gastric surgery, was a renowned musician and the confidant of Johannes Brahms. Fritz Kreisler forsook the career of medicine to enter the concert field.

This book is a compilation of fascinating stories, with considerable newsy small talk of lesser lights and the contemporaries of the world's great musicians of the 17th, 18th, and 19th centuries. Accounts are given about the less famous forerunners and companions of Mozart, Haydn, and Beethoven. Chats on Scarlatti and Vivaldi and notes on the early operas in Vienna, Paris, Rome, Milan, and Naples depict behind the scenes intimacies and gossip tidbits. The jealousies and human frailties of small and great alike are revealed in readable style.

The 18th century was a time of memoirs, confessions, and autobiographies that revealed the background and development of musicians of lesser rank. Karl von Dittersdorf was a popular and prolific composer; Frank Benda, the violinist, was the leader of the orchestra that performed before the Prussian crown prince, Frederick II. Important data are revealed concerning Christian Gottlieb Neefe and Johann Baptist Schenk, who were teachers and colleagues of Beethoven. Much little-known material, heretofore obscure, is included. There are comments on the backgrounds of Offenbach and Meyerbeer, and a chapter on Johann Stamitz, once called the Shakespeare of music. The Czech predecessors of Franz Schubert, Johann Tomaschek, and Hugo Vorisek become alive in their controversies and performances. There is an enlightening chapter on the anonymous Jewish musicians of the 17th century, who journeyed from town to town and were the forerunners of Bohemian music.

New light is shed on the background of the waltz. Schmelzer is designated as the first Viennese dance composer, the Johann Strauss of the Baroque. A detailed account of the visit to America, some 80 years ago, of Frantz Abt and Johann Strauss relates their reaction to the musical conditions prevailing in America at that time. In a letter written by Abt from Washington, reflections on activity in social and political circles furnish highly interesting reading material.

There are newsy essays and intimate descriptions of the tones and artistic accomplishments of the castrati, the eunuchs who were popular in the early 18th century in Europe and the Mediterranean countries.

A chapter on musical monarchs discusses a number of performers and music lovers who attained prominence in the political forums of world history; an example is Paderewski, the composer-pianist, president of Poland. Thomas Jefferson was said to have loved to play the violin, although gossips labelled him the worst performer in Virginia. The musicians of ancient royalty included King David, whose political fortunes were greatly enhanced when he charmed King Saul's court with his harp. The Roman emperor Nero placed his love of music above the safety of his people. Devotion to music marked the rulers of many courts and principalities. It was the custom to school children of the court in musical graces; examples of this are Queen Elizabeth, the Hapsburgs of the Renaissance, and numerous court musicians.

The book is divided into two parts; the first part is devoted mainly to discussions of forgotten groups of musicians, such as the old Jewish minstrels, and individual musicians. The second part consists of intimate self sketches and autobiographical notes of musicians who made their mark locally, and, for the most part, significantly influenced the works of major composers. At the end of this interesting volume, there is a series of notes to the autobiographical text that should prove important to those who delight in searching the archives and hidden recesses for new light on artists who have created, in tones of beauty and rhythm, compositions that they hoped would prove of enduring value.

American Pharmacy: Fundamental Principles and Practices, Pharmaceutical Preparations. [Volume I]. Editor-in-chief: Rufus A. Lyman, M.D. Advisory editors: James M. Dille, Ph.D., Professor of Pharmacology, University of Washington, Seattle, and others. Consulting editor: George Urdang, Ph.G., D.Sc.Nat., Sc.D.(H.C.), Director, American Institute of History of Pharmacy, Madison, Wisconsin. Third edition. Cloth. \$8. Pp. 505, with 192 illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; Aldine House, 10-13 Bedford St., London, W.C.2; 2083 Guy St., Montreal, 1951.

The first edition of volume 1 of this text represented a new trend in pharmaceutical textbook construction. Rather than duplicate the encyclopedic approach that characterizes the makeup of similar texts, the editors made an effort to present individualized discussions of the fundamental principles and practices of pharmacy and the various official or accepted preparations to which they apply. These were contributed by various specialists who are both research workers and teachers in their respective fields. The wide acceptance that this book has received is testimony to the wisdom of this treatment of the subject matter.

This edition is divided into two parts and 30 subdivisions, with an introductory survey of the history, present status, and future potentialities of the profession of pharmacy. Part I is devoted to fundamental principles and processes, such as the various manipulative procedures employed in the extraction, purification, preparation, preservation, and packaging of drugs. Part 2 deals with the various classes of pharmaceutical preparations, their characteristics and uses. A short but representative list of references accompanies the discussion of each class. This edition features rearrangement of some subject matter and changes in terminology and types of preparations that were needed to bring the book into accord with the 14th revision of the United States Pharmacopeia, the 9th edition of the National Formulary, and New and Nonofficial Remedies, 1951.

The American Academy of Orthopaedic Surgeons Instructional Course Lectures. Volume VIII, 1951. Editor: Charles N. Pease, M.D.; associate editor: Sam W. Banks, M.D. Cloth. \$8.50. Pp. 356, with illustrations. J. W. Edwards, 1745 S. State St., Ann Arbor, Mich., 1951.

This volume meets the high standards set by the previous instructional course lectures. The authors are eminent orthopedists and are authorities on the subjects of their lectures. The material is based, for the most part, on the authors' experiences and has some value as a reference. It is, however, difficult to read, since there is little or no continuity of subject matter.

The purpose of the book is to preserve a series of valuable lectures that were selected from lectures given at the American Academy of Orthopaedic Surgeons in January, 1951. It is an excellent selection of timely subjects of current interest. The illustrations and plates are clear, and there is a bibliography following each article. The style of writing varies with each lecturer. This series of lectures includes a complete symposium on medullary fixation of the femur and on cortisone and corticotropin. In addition to the symposiums, there are twenty lectures on diverse orthopedic subjects. These range from basic subjects, such as human development in growth to others as specific as radioisotopes. The general format is good, and the volume a convenient size.

Surgery of the Oblique Muscles of the Eye. By Walter H. Fink, M.D. Cloth. \$8.75. Pp. 350, with 93 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1951.

This monograph, summarizing current knowledge on the superior and inferior oblique muscles of the eye, includes not only the author's extensive personal experiences and research but also an extensive discussion of the entire literature on the subject. Until recently these muscles were forbidden territory to the ophthalmic surgeon, who confined his operative procedures on the extraocular muscles to the four recti. Because of increased interest in the subject, this volume is particularly timely, and, although certain aspects of oblique surgery are still controversial, a book of this type does much to crystallize ophthalmic understanding and practice. There is a full discussion of the embryology, comparative anatomy, developmental anomalies, microscopic and gross anatomy, and surgical anatomy of the oblique muscles, in the first section of the book. The second part deals with the management of oblique muscle defects and includes

discussions on etiology, physiology, diagnosis, surgical indications, and surgical techniques. The last-mentioned topic is well illustrated and described. An appendix deals with the anatomical considerations in operations for retinal detachment. Although apparently unrelated, this was added because of the importance of the muscles to the surgical anatomy of detachment surgery. The author's extensive anatomic studies on the oblique muscles, especially as related to their fascial connections and variations in insertion, make this volume especially authoritative. It is a necessary addition to the library of any ophthalmic surgeon interested in this field.

The Nature and Treatment of Mental Disorders. By Dom Thomas Verner Moore, O.S.B., Ph.D., M.D., Professor of Psychology and Psychiatry, Catholic University of America, Washington, D. C. Foreword by Edward A. Strecker, M.D., Professor of Psychiatry, Graduate and Undergraduate Schools of Medicine, University of Pennsylvania, Philadelphia. Second edition. Cloth, \$5.50. Pp. 362. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1951.

This book discusses the need for a sound psychology and psychopathology of mental disorders that parallels present information in physiology and pathology; thus making a true insight into somatic disorders possible. Much of the investigative work discussed is based on studies that were aided by a grant from the Rockefeller Foundation to the Catholic University of America for investigations in the field of psychiatry. The author discusses the fundamental concepts of psychopathology as expressed by Freud, Adler, Jung, and Alexander, and attempts to classify each scientist in accordance with what he feels to be that scientist's ideas of value and the areas in which he believes such concepts are lacking. In discussing specific psychiatric entities, the author places more value on the Kraepelinian diagnostic classification than is generally credited to it by most of the advanced schools of psychiatry.

In the appendix, there is a classification and definition of clinical entities in psychiatry as they are given in the third edition of "Standard Nomenclature of Diseases and Operations." This has now been outmoded by the appearance of the fourth edition of "Standard Nomenclature," in which the classification of diagnostic entities is radically changed. Sections of the book on techniques of therapy are illustrated by a wide variety of case histories drawn from the author's experience. The case material discussed and the interpretations provided by the author should be of considerable interest to the clinician and student.

Thematic Test Analysis. By Edwin S. Schneidman, Ph.D., Clinical Psychologist, Veterans Administration Neuropsychiatric Hospital, Los Angeles, California. With collaboration of Walther Joel, Ph.D., Assistant Chief Clinical Psychologist (Psychotherapy), V. A. Neuropsychiatric Hospital, Los Angeles, and Kenneth B. Little, Ph.D., Clinical Psychologist, V. A. Hospital, San Francisco. Foreword by Henry A. Murray, M.D. Cloth. \$8.75. Pp. 320, with 3 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1951.

This book represents what is probably the most extensive psychological "dissection" ever performed on a human being. Its major purpose is to present a round table of interpretations by several experts of one person's psychological test data. This person's responses in the thematic apperception test and the "make a picture story" test were sent to experts who have published techniques for analyzing the former. Besides the responses, the experts were given only the subject's age, sex, and marital status. Each was asked to analyze the two tests by his own method and to return the recorded steps of his working procedure, such as working notes, notations, and tabulations, as well as the final write-up of his analysis. Sixteen of the experts responded, and the result is this presentation of the main techniques now being used in interpretation of these two tests in research and clinical work. The book also contains other test protocols for the same person, each protocol being interpreted by an expert on that particular test. These tests are the Rorschach, the Wechsler-Bellevue Intelligence Scale, the Minnesota Multiphasic Personality Inventory, the Draw-a-Person test and the Bender-Gestalt figures test. In addition, the author has provided historical and clinical data on the subject.

This book is of particular value to the novice in thematic test analysis, for, besides indicating some of the major principles of thematic test interpretation, it makes comparisons between many of the published techniques much easier. For one who is more

familiar with projective techniques, the book permits comparisons between the interpretations of thematic tests and those of other tests, and between thematic test interpretations and actual case history and psychotherapy data. It is difficult to say whether implications derived from this book have valid application to personality theory, since the research reported in it has several real limitations. First, the entire research revolves around one person. In addition, all interpretations were made by "blind analysis"; this, of course, was necessary in order to determine what valid information can be derived from the test data alone. It is interesting to note that, while the validity of blind analysis is regarded with great suspicion by most experts, these analyses show a high degree of correspondence, and they correlate well with the behavioral data. In spite of the limitations that such research must have, the book will be of great value to anyone interested in projective psychology.

Renal Pelvis and Ureter. By Peter A. Narath, M.D., F.I.C.S., Adjunct Professor of Urology, New York Polyclinic Medical School and Hospital, New York. Cloth. \$12.50. Pp. 429, with 264 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1951.

In this book, the author has assembled results of his studies in renal anatomy, histology, and physiology, which he has carried on over many years. His most important contributions concern the renal papillae, the calyces, and the pelvis. He has provided a new conception of the circumpapillary portion of the minor calyces and the fornix and its role in absorption and resorption. The graphic description of its various functions and the different types of deformity caused by disease or trauma are interesting. Although many of the author's deductions are based largely on urographic interpretation, they apparently have a factual basis. There are those, however, who differ with some of the hypotheses. The chapter on dynamics of the upper portion of the urinary tract reveals many details of physiological activity in this area that have not been clearly understood. The chapters dealing with resorption and absorption in the calyceal area and the difficult interpretation of extra pelvic urographic shadows caused by overdistention of the renal pelvis are of exceptional interest. The graphic illustrations are outstanding. In the chapter on tonic conditions (tonus) in the urinary tract, the author discusses a subject that has received insufficient attention. He refers to the evidence of spasticity as well as hypotony occurring in the urinary tract as ascertained by urographic and cystoscopic studies. Wide variations in tonicity are observed in reflex action caused by instrumentation and trauma. Variation in elasticity of the urinary tract is shown by the surprising degree of expansion, particularly in the outline of the fornix when overdistended. In his discussion of anatomic variations of the ureter, the author states that ureteral division (fissus) is the result of splitting in the ureteral anlage. He maintains that if one branch of the ureter remains undeveloped and ends in a blind sac, the term ureteral diverticulum is inaccurate. Readers of this book will find the contents informative and stimulating. They will be given a somewhat different concept of calyceal-pelvic excretory function than is generally held.

Atlas der normalen Histologie und mikroskopischen Anatomie des Menschen. Von E. von Hertath, o. ö. Professor der Anatomie an der freien Universität Berlin, und S. Abramow. Cloth. \$11.25. Pp. 139, with 398 illustrations. Georg Thieme, Diemershaldenstrasse 47, (14a) Stuttgart O; agents for U. S. A., Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1950.

The title of this book implies that it is an atlas of the normal histology of the human body and is published in the German language. It is a collection of 398 photomicrographs, mainly in color, each with a descriptive legend; however, many of the illustrations are of animal tissues other than those of the human body, and some are of diseased tissues. All of the legends are brief and comment only on the material actually illustrated. There is no correlating descriptive text to integrate the illustrations and give the student of histology the basic elements necessary to understand the structure of the various tissues of the body. A student beginning the study of the normal histology of the human body would need other texts for this information. The atlas, accordingly, provides only supplemental help and probably has small appeal to students of histology in this country.

Las afecciones del hígado, de las vías biliares y del páncreas. Por Raul A. Piaggio Blanco y Carlos M. Sanguinetti. Tomo I, primera y segunda partes: Exploración funcional del hígado y de las vías biliares; síndromes clínicos. Tomo II, tercera parte: Semiología clínica y radiológica del hígado y de las vías biliares; afecciones del hígado. Paper, Pp. 817, with 82 illustrations; 462, with 69 illustrations. Imprenta "Rosgal," Hilario Rosillo, Calle Ejido 1624, Montevideo, 1951; 1948.

This book thoroughly discusses the pathological entities affecting the liver and biliary passages. Volume one, which is divided into two parts, deals with the functional exploration of the liver and biliary passages and clinical syndromes. Analysis of the various methods used by the authors would take one too far afield; it is sufficient to say that discussion of the physical examination of affections of the liver and biliary passages embrace all known tests and methods. The second volume, which consists of part three of the complete work, deals with the semiology, radiology, and clinical aspects of diseases of the liver and biliary passages. The text is thorough; for example, in the section on the liver and diverse affections the following entities are discussed: the pathology of the liver in pernicious anemia (Biermer's disease) and in polycythemia vera (Vaquez-Osler disease), the effects of the leukemias in diseases of the liver, and the pathological changes in the liver in diseases of the endocrine glands, such as the thyroid.

Experimental studies, pathology, anatomy, symptomatology, and treatment are discussed at length; however, although medical therapy is outlined, surgical operations are completely omitted. The various forms of jaundice are thoroughly analyzed. The correlations of diseases of the biliary passages and the pancreas are evaluated from every point of view. This is an excellent work that is completely up to date. Those who read Spanish will find it a valuable source of information. The index is comprehensive and thorough. The illustrations, consisting of microphotographs, radiographs, and sketches, are well executed. The work is highly recommended to those interested in affections of the liver and biliary passages.

The Organization of Bones. By P. Lacroix, Professor in Faculty of Medicine, University of Louvain, France. Translated from amended French edition, by Stewart Gilder, B.Sc., M.B. Cloth. \$6. Pp. 235, with 87 illustrations. Blakiston Company (division of Doubleday & Company, Inc.), 1012 Walnut St., Philadelphia 5; J. & A. Churchill Ltd., 104 Gloucester Pl., Portman Sq., London, W.1, 1951.

In this valuable monograph, the author describes the behavior and growth of epiphyseal cartilage, bone, periosteum, and marrow in a clear and interesting manner. His observations are based on extensive, original experiments. Discussions, which are to the point, reveal an understanding of the extensive writings of other investigators. His experiments, designed to study the behavior of epiphyseal cartilage, bone, periosteum, and marrow are interesting. The implantation of the tissues under study beneath the capsule of the kidney circumvents the pitfalls of other techniques of experimental observation. Numerous, excellent illustrations supplement the text, and an extensive up-to-date bibliography is included. This small volume contains much information on all aspects of bone organization and growth and should be read by clinicians as well as biologists, anatomists, and embryologists. One rarely encounters monographs that are as instructive and thought provoking as this book.

French-English Science Dictionary for Students in Agricultural, Biological, and Physical Sciences with a Supplement of Terms in Aeronautics, Electronics, Radar, Radio, Television. By Louis De Vries, Professor of Modern Languages, Iowa State College, Ames. With collaboration of members of Graduate Faculty. Second edition. Cloth. \$6.50. Pp. 596. McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 18; Aldwych House, Aldwych, London, W.C.2, 1951.

The first section of this edition is essentially the same as the first edition, with minor revisions and corrections in the original text for greater accuracy. The second section is a supplement, which will greatly enhance the value of the volume to most users. In this supplement, there have been included words, terms, and expressions that have come into use as a result of recent developments in the fields of aeronautics, electronics, radar, radio, and television.

QUERIES AND MINOR NOTES

BASKETBALL IN JUNIOR HIGH SCHOOLS

TO THE EDITOR:—The chairman of our junior high school study group approached me in regard to obtaining your opinion on the effect of competitive basketball on the health of boys from 11 to 14 years of age. Many parents are eager to have their boys engage in competitive sports, and many others feel that such play is detrimental to the health of growing boys. I would appreciate an opinion on this subject.

John W. Conklin, M.D., Platteville, Wis.

ANSWER.—When basketball is appropriately modified to meet the needs of this younger age group, there is no reason why those who are found to be fit by medical examination should not participate under proper control. An intramural program that stresses opportunity for all students to play against others of about equal ability, age, height, and weight is recommended. An interschool program of the "varsity" type, which generates pressures that may cause immature youths to overtax themselves or that limits participation to a few, is not recommended. For this age group, shorter quarters, more frequent time-outs, and other suitable modifications in rules are strongly urged. Other suggestions that will help to make participation safe and healthful were adopted by the National Joint Committee on Standards for Boys Athletics and were endorsed by the Joint Committee on Health Problems in Education of the National Education Association and the American Medical Association:

1. A health examination should be required previous to participation, preferably on a seasonal basis, with annual examination a minimum requirement.
2. A physician should be present at all contests involving activities where the injury hazard is pronounced.
3. A contestant who has been ill or injured should be readmitted to participation only on the written recommendation of a physician.
4. A contestant upon returning to participation after illness or injury should be carefully observed, and if there is any doubt as to his condition he should immediately be referred to a physician.
5. The coach (faculty member in charge) should be competent in first aid and thoroughly versed in sports conditioning and training. It is also strongly recommended that all players be given basic instruction in first aid.
6. In case of head, neck, or spine injury, or suspicion thereof, the player should be removed from play, placed at rest, and be given the immediate attention of a physician.
7. Every school should have a written policy regarding the responsibility for injury incurred in athletics, and this policy should be known to all participants, their parents, and other responsible adults. Arrangements should be made for obtaining and paying for medical and hospital care of injured participants, in accord with local policy.
8. The best obtainable protective equipment should be provided for all participants, and special attention should be given to proper fitting of such equipment.
9. Competition should take place only between teams of comparable ability, and playing seasons should be limited to reasonable duration.
10. No preseason games should be played until players are well drilled in fundamentals and have had a minimum of two weeks of physical conditioning.
11. Playfields should meet standard requirements for size of area, playing surfaces, and facilities for safety, and all reasonable precautions should be taken to prevent accidents.
12. Contests should be selected, and rules and lengths of playing periods should be such that they will not overtax the physical abilities of the students concerned.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

POSTPARTUM DEPRESSION

TO THE EDITOR:—I have noticed a postpartum depression in many of my patients. They complain of excessive fatigue, mental apathy, loss of vigor, and loss of sexual desire. Physical examination shows nothing unusual. All had uneventful pregnancies and deliveries. This state lasts, in most cases, well over a year or two. In the patients that become pregnant again it disappears, and they feel better than ever. I would like an explanation of this condition.

Abraham D. Cohen, M.D., New City, N. Y.

ANSWER.—Several factors must be considered in answer to these questions. A poor diet (one lacking in proteins, minerals, and vitamins) during and after pregnancy leads to nutritional deficiencies and, in some patients, symptoms of fatigue, exhaustion, and mental apathy. Many patients in this postpartum period, because of apprehension for the new baby, increased work, and frequent loss of rest, develop an actual physical fatigue and fail to recuperate properly.

There is much psychic trauma involved in pregnancy and the postpartum period that often is not appreciated by husband and physician. Unless the patient has help and understanding during this period, she may be slow to recover, or may even become psychotic. Following delivery of the baby, there is usually a shift of love and affection solely to the baby. During this period the woman may be apathetic, show little interest in the rest of the family, and would certainly lack sexual desire. After a short interval there occurs a natural redirection of part of her affection toward the husband and other children. Finally, there is a more specific reason for this state of mind and behavior, namely, lowered estrogen production. During pregnancy there is a considerable increase in estrogen production, and, theoretically at least, this is supposed to account for the feeling of well-being in the pregnant woman. This should occur only in women whose estrogen production is ordinarily deficient. A woman with normal estrogen balance usually does not feel better with an increase in estrogen. Often the explanation is simple and the condition easily corrected if the above factors are properly evaluated.

LOBOTOMY VERSUS INJECTION OF FRONTAL LOBE

TO THE EDITOR:—Instead of radical lobectomy for mentally ill patients, can the offending lobe be treated with alcohol injections made through small holes in the patient's skull, and, if so, with what degree of success? To what extent is lobectomy being performed, and what are the results and the mortality rate?

M.D., Virginia.

ANSWER.—Frontal lobectomy has rarely, if ever, been used in the treatment of mental disease. The operation most commonly used is frontal lobotomy, a procedure in which a variable part of the white matter in the centrum ovale of the frontal lobe is divided in the plane of the coronal suture. Some surgeons have removed the superior part of the anterior portion of the convexity of the cortex of the frontal lobe, an operation termed topectomy; others have undercut various parts of the frontal cortex. Frontal lobotomy is usually carried out through a small trephine opening on either side of the skull, either under direct vision or blindly. No reliable figures are available as to the number of operations performed, although the total probably runs in the tens of thousands. The results of these procedures vary with the type of operation and with the nature of the patient's disease. Those interested should consult Freeman and Watts' "Psychosurgery in the Treatment of Mental Disease" (Springfield Ill., Charles C Thomas, 1951) for a discussion of this matter. The mortality rate of any of these procedures does not exceed 1 to 2%; in many instances, there is no mortality. Interruption of the white matter of the frontal lobe by the injection of alcohol into the brain was carried out by Moniz and his associates in at least 10 of his earliest cases. These are described in detail in his book ("Tentatives opératoires dans le traitement de certaines psychoses," Paris, Masson & Cie, 1936). Moniz in-

jected alcohol into the centrum ovale of both frontal lobes. He injected 0.1 or 0.2 cc. with each injection and made from 1 to 10 injections in each frontal lobe, distributing the injections in various patterns. Moniz soon gave up this procedure because of unsatisfactory results and adopted the surgical division of the white matter of the frontal lobes. More recently, Van Wagenen and his associates injected procaine (novocaine®) into the white matter of the frontal lobe as a preliminary and temporary procedure in an effort to estimate, in advance, the possible results of frontal lobotomy.

TREATMENT OF POSTPHLEBITIC ULCER

TO THE EDITOR:—A 43-year-old white woman, in excellent health, had a bilateral, postpartum saddle thrombophlebitis in 1942. She was given bishydroxycoumarin (dicumarol®) and had an uneventful recovery. Since then, there have been occasional episodes of ankle edema that subside with rest and elevation of the ankle. In 1950, after an insect sting, a small ulcer developed on the inner side of the right leg, 5 cm. above the malleolus. A year later, after arterial involvement was ruled out, she began soaking her leg for short periods in magnesium sulfate, applying aureomycin ointment, 3%, locally, elevating her legs during the day, and elevating her legs to a 45° angle during the night. After two months, the ulcer healed, leaving a white, thin scar, and all therapy was discontinued. In a month, however, after a few days of strenuous walking, the ulcer broke again. What other suggestions can you make for firm healing and permanent cure, and what is your opinion of the cruricast (Unna's paste) treatment?

M.D., New York.

ANSWER.—This patient has a chronic recurrent postphlebitic ulcer. If there are visible varicosities, one can test for the presence of saphenous perforator or deep venous insufficiency, and, depending on the result of such tests, a stripping of the superficial venous system or a division of the popliteal vein may be indicated. If lymph stasis is predominant and there are large indurated areas around the ulcer, glycerin-gelatin casts are helpful, and later, if the ulcer is intractable, a wide excision of the ulcer, followed by a split-thickness skin graft, should be made. If the ulcer is painful, the skin around it moist and cyanotic, and the pulse rate diminished, a lumbar sympathectomy will relieve this causalgic state. It is likely that elastic compression will be needed for a long time and that residual edema will be permanent. (For a more detailed analysis of the problem, the following references should be consulted: Ochsner, A., and De Bakey, M.: Postphlebitic Sequelae, *J. A. M. A.* 139:423 [Feb. 12] 1949, and de Takats, G., and Graupner, G. W.: Division of the Popliteal Vein in Deep Venous Insufficiency of the Lower Extremities, *Surgery* 29:342, 1951.)

LOBECTOMY AND ASTHMA

TO THE EDITOR:—I am gathering data on lobectomy performed in patients with chronic bronchial asthma complicated with bronchiectasis. Lobectomy mortality, when the operation is performed by competent thoracic surgeons, according to Cecil (*Textbook of Medicine*, Philadelphia, W. B. Saunders Co., 1947, ed. 7, p. 932) is 5% or less. Would chronic asthma increase the operative risk?

M.D., Texas.

ANSWER.—The number of cases of lobectomy performed in patients with chronic bronchial asthma complicated by bronchiectasis is insufficient to establish mortality rates on a statistical basis. It is safe to say, however, that an increase in operative mortality can be anticipated in patients with severe asthma. The decision as to whether to recommend operation to patients with complicating asthma would depend largely on the severity of the bronchiectasis. Another factor to be considered is that bronchiectasis may serve as a trigger mechanism in aggravating attacks of asthma. This mechanism is probably caused by severe coughing, and, in some cases, if the bronchiectatic lung tissue is removed, the asthma is improved. Another factor that must be carefully evaluated is the degree of associated emphysema. If the lungs are severely damaged by emphysema, the mortality rate from pulmonary resection can be expected to increase sharply.

COMBINED ALCOHOL AND BARBITURATE INTOXICATION

TO THE EDITOR:—A woman, aged 45, weighing 80 kg., was found dead. Chemical analysis of her blood revealed that it contained ethyl alcohol, 0.27% by weight, and barbituric acid derivative, 2.65 mg. per 100 cc. Do these data provide an explanation of her death? Would either of these substances alone be the probable cause of her death? Assuming the patient was intoxicated from ethyl alcohol, what would the theoretical minimal concentration of barbituric acid derivative (especially pentobarbital sodium) have to be to account for her death? Please give me authoritative references on this subject?

M.D., New Hampshire.

ANSWER.—The presence of both 0.27% ethyl alcohol by weight and 2.65 mg. per 100 cc. of barbituric acid derivative in a postmortem sample of this woman's blood constitutes a plausible explanation of her death, despite the fact that neither substance alone was present in a fatal concentration. A blood alcohol value of 0.27% by weight is well above the threshold for intoxication (about 0.15%) and is considerably below what is ordinarily considered to be a fatal concentration (about 0.50%). The significance of the barbiturate concentration is more difficult to appraise. A blood concentration of 2.65 mg. per 100 cc. following the ingestion of a slow-acting form of the drug, such as barbital or phenobarbital, would not of itself be dangerous and probably would not even cause loss of consciousness. However, such a blood concentration following the ingestion of a rapidly acting compound, such as secobarbital sodium (seconal®) or pentobarbital sodium, might well account for profound depression and deep coma independently of any other factor (Fisher, R. S.; Walker, J. T., and Plummer, C. W.: Quantitative Estimation of Barbiturates in Blood by Ultraviolet Spectrophotometry: II. Experimental and Clinical Results, *Am. J. Clin. Path.* 18:462-469 [June] 1948). Thus it appears that this woman may have ingested more than half a fatal dose each of alcohol and a barbiturate. Since the pharmacological effects of these two substances tend to be additive (Jetter, W. W., and McLean, R.: Poisoning by the Synergistic Effect of Phenobarbital and Ethyl Alcohol: An Experimental Study, *Arch. Path.* 36:112-122 [July] 1943) it is plausible to attribute her death to the combined effects of alcohol and barbituric acid intoxication.

MYXOMA NEAR THE HEEL

TO THE EDITOR:—A patient had a lump just anterior to the Achilles tendon at the level of the calcaneus that extended laterally. This mass, which looked like a lipoma, had been present for two years. As it had grown a little in the last few months I excised it. It did not shell out particularly well, and I had to use sharp dissection to free it from the superior, posterior surface of the calcaneus and the Achilles tendon. Although I removed very little of the Achilles tendon, I had to excise some of the periosteum. The pathological diagnosis was myxoma. Is further treatment indicated? Should wider surgical excision, such as removal of the Achilles tendon or the upper portion of the calcaneus, be performed, or should roentgen ray therapy be used?

M.D., Oklahoma.

ANSWER.—Myxoma is a tumor not uncommonly seen about the joints and in regions such as described in this case. Pathologically, the tumor is in the twilight zone between benignancy and malignancy, and for this reason its course may be unpredictable. However, even though histological evidence of malignancy may be difficult to demonstrate, the malignancy of the tumor should always be considered as being of low grade. Although the tumor is usually very troublesome as far as local recurrence is concerned, the danger of regional or distant metastasis is not great. For this reason, if thorough local excision has been done, one can safely wait to see what develops. It is possible that the lesion may have been removed completely. Should local recurrence result, a second attempt to excise the lesion should be made. If complete removal is impossible, amputation should be considered. Myxomas are extremely radiosensitive, and for all practical purposes roentgen therapy is of no value in their treatment.

CYANIDE CONTAMINATION AND WOUND HEALING

TO THE EDITOR:—I have been asked by an industrial plant that uses a cyanide preparation for polishing steel to suggest a method of treatment for small slow-healing wounds for use in the plant's first aid department. I have suggested washing the wounds thoroughly with hydrogen peroxide solution. Have you any information on this subject?

John T. Bate, M.D., Louisville, Ky.

ANSWER.—Soluble cyanide salts are not likely to retard wound healing. Furthermore, they could be readily removed from a wound by washing it with sterile water or isotonic sodium chloride solution.

Contamination with relatively insoluble metallic salts of cyanide might interfere with wound healing. Hydrogen peroxide washing solution may not prove effective against these. Sodium hypochlorite in alkali solution would eliminate the cyanide but might prove as irritating to the skin as the cyanide itself. Potassium permanganate solution, although efficacious, would lead to unwanted skin coloration. A suitable measure for prevention of cyanide dermatitis after exposure, but not necessarily an appropriate treatment for the dermatitis, is washing of the wound with any nonirritating synthetic detergent having a pH value below 7. Two such preparations obtainable commercially are "pH6" and acidolate.²⁰ These preparations liberate the cyanide in the form of hydrocyanic acid, but the quantity of acid thus produced has no toxic effect.

RADIOACTIVE IODINE, PROPYLTHIOURACIL, AND THYROTOXICOSIS

TO THE EDITOR:—Propylthiouracil, 50 mg. four times a day, was administered in April, 1950, to a 54-year-old white woman because of thyrotoxicosis. The initial basal metabolic rate was +28%. The clinical response to propylthiouracil has been excellent. How long should the propylthiouracil be administered in a case of this type to effect a permanent cure?

M.D., Illinois.

ANSWER.—If the patient has a nodular goiter with hyperthyroidism, a subtotal thyroidectomy should be performed after adequate preoperative preparation. If the patient has exophthalmic goiter, treatment with radioactive iodine should be considered. It is superior to propylthiouracil because the chances of producing a permanent remission are much greater; in fact, permanent remission can be produced in as high a percentage of patients with the use of radioactive iodine as with a subtotal thyroidectomy. Propylthiouracil produces a permanent remission in approximately 50% of the patients. The data available are not too good, but the percentage is certainly no higher than this. It is apparently necessary to maintain the basal metabolism at the normal level for at least a year before treatment is stopped, in order to produce a permanent remission, and, even after this period, relapses are common.

EXERCISE AND TUBERCULOSIS

TO THE EDITOR:—In a patient with minimal pulmonary tuberculosis who has responded well to several months of bed rest and who is afebrile, how much temperature elevation above 98.6 F could be expected to occur after walking about 500 ft. in 15 minutes? If a healthy person were put on bed rest with bathroom privileges for five months, how much temperature elevation, if any, would the above exercise be expected to produce?

M.D., North Carolina.

ANSWER.—In the first place, such patients should not be allowed to get out of bed and walk 500 ft. This would almost surely liberate enough nontuberculous toxins to cause an abnormal rise in temperature; however, it would be difficult to determine the type of the toxins. Exercise should be more gradual. Except at the ovulation time in women, a temperature above 99 F is considered pathological. There is a liberation of toxins from the lesions, with an effect on the heat control centers. Even after five months' bed rest with bathroom privileges, a normal person should not have an abnormal temperature until he becomes fatigued; then, it is conceivable that an abnormal temperature may result.

A MOTHER OF TWO MONGOLOID CHILDREN

TO THE EDITOR:—A man aged 38 is married to a woman of 34 who has had three normal children by a previous marriage. A child born from the second marriage was mongoloid. The mother of the wife had two normal children and two mongoloids. What is the likelihood of this couple having a normal child?

M.D., New York.

ANSWER.—The birth of a second mongoloid child is rare, occurring in between 1 and 2% of such families. On the other hand, mongolism has been observed in all three children in one family. There is no information available regarding the chance of mongolism occurring in two successive generations. The cause of the condition is unknown. Mongolism occurs most frequently when the parents are relatively late in their reproductive lives. The preceding pregnancy frequently terminates in abortion or miscarriage, and in many instances, the birth of a mongoloid child is preceded by an unusually long period of involuntary sterility. The prospective parents have reached the period in their respective reproductive lives in which mongolism is likely to appear. No one can predict the outcome of any future pregnancy with respect to the chance that any future child will be a mongol; however, the couple in question have a greater chance of this occurring than they would if both of them were in their early twenties. On the other hand, their chances of having normal children are greater than their chances of having mongoloid children, regardless of the fact that their first child was mongoloid.

MILK FROM COWS GIVEN BRUCELLA VACCINE

TO THE EDITOR:—A dairyman has given active (live bacteria) brucellosis vaccine to cows previously tested and found to be negative to the disease. Is it possible for persons drinking milk from cows so treated to contract brucellosis? If so, how much time should elapse before the milk is safe to drink? Is there a test for the cows or their milk to determine if the milk is safe to drink?

C. C. Horton, M.D., Pendleton, S. C.

ANSWER.—It is presumed that the dairyman in question has immunized his cattle with strain 19. This is a viable, but avirulent strain of *Brucella abortus* that has been widely used for protecting cattle against *Brucella abortus*. There is no evidence that human beings have ever contracted brucellosis by drinking milk from cows immunized in this manner. There are two widely used tests for determining if cows have brucellosis and are excreting *Brucella* in their milk. The first is the blood agglutination test, and the second is the ring test, which is an agglutination reaction performed on whole milk. If an elevated titer of *Brucella* agglutinins is present by either test, this suggests that the cows have the active disease and may be excreting *Brucella* in their milk. The consumer of such milk is only protected by proper pasteurization. On rare occasions, cows may excrete viable *Brucella* in their milk and yet have a negative blood agglutination test. If one is living in an endemic area of brucellosis, only pasteurized milk should be used for human consumption.

PERTUSSIS VACCINE

TO THE EDITOR:—I have seen several children under 1 year of age, who, on exposure to whooping cough, were given three or four weekly injections of pertussis vaccine (prophylactic). It has been my understanding that this would be more harmful than beneficial.

Jackson Herbert, M.D., Portsmouth, Ohio.

ANSWER.—The pertussis vaccine now in general use is not ordinarily recommended for administration after exposure to whooping cough, because there would be insufficient time to build up immunity. Furthermore, it might be contended that such a procedure would be harmful. This is based on the theory that, with active immunization, there may be a negative phase after the first injection that would result in increased temporary susceptibility. Highly concentrated human hyperimmune pertussis serum is sometimes used successfully for passive immunization after exposure to whooping cough.

SEIZURES IN AN EMOTIONAL WOMAN

TO THE EDITOR:—*A patient, when becoming emotionally upset, is subject to spells, in which she loses complete control of her muscles. She says she feels like all her bones were suddenly removed. She is conscious during these seizures and is completely aware of her surroundings, but is unable to move or to speak. Only striated muscles seem to be affected since there is no history of incontinence. She avoids walking down stairways and holding small babies, because, when she has an attack, she collapses in a heap. These attacks last sometimes for a moment and sometimes for a few minutes. She is unable to bring one on, even though she has tried on several occasions. These seizures are always preceded by an aura, consisting of inability of the eyes to focus, blurring vision, and eyes crossing. There is no pain. Following them, she usually feels more relaxed and more at ease than before. Blood pressure was 140/90 at last examination. Epilepsy has been suggested as a possible cause, but an electroencephalogram was entirely within normal limits. What is your advice?*

Oscar H. Neumann, M.D., Prosser, Wash.

ANSWER.—The normal electroencephalogram does not rule out epilepsy, but astatic (drop) seizures are rare in adults and are not followed by inability to move. Symptoms of collapse that are precipitated by surprise or emotion suggest the cataplectic attacks of narcolepsy. Such patients may also experience inability to move or speak on awaking or falling asleep; however, abnormalities of sleep are not mentioned for this patient. The fact that the attacks are preceded by agitation and followed by relaxation suggests hysteria. Principally in favor of some organic cause is the preliminary incoordination of ocular muscles. A paroxysmal disturbance in the midbrain area, whether pathological or not, would explain the symptoms but would not specify a diagnosis. Therapeutic trial could be made of dexedrine® (d-amphetamine sulfate), 10 to 30 mg. a day, of trimethadione (tridione®), 0.9 gm. a day, or of psychotherapy.

UTERINE DISPLACEMENTS

TO THE EDITOR:—*In what percentage of the cases of uterine displacement is surgery performed?*

Edwin Matlin, M.D., Mount Holly Springs, Pa.

ANSWER.—The exact percentage of cases in which surgery is done for uterine displacements is not known, but in the opinion of most gynecologists, it is too high. Most gynecologists believe that retroflexion and retroversion of the uterus usually produce no symptoms and require no treatment. About 20% of all women have a retrodisplaced uterus, and most women if not told about it are not aware of any untoward symptoms.

An operation should never be performed for uterine displacement that does not produce symptoms. Even in the presence of symptoms, such as backache, bearing-down pains, dysmenorrhea, and leukorrhea, an operation should not be performed until a therapeutic test has been made. To accomplish this, a properly fitting pessary is inserted in the vagina, with or without first elevating the uterus. If symptoms disappear while the patient wears the pessary, and if they reappear when the pessary is removed, an operation is indicated. If this test is made, it will be found that relatively few women with a retrodisplaced uterus require an operation. In rare cases, a suspension operation may be justified to overcome sterility.

WEIGHT REDUCTION

TO THE EDITOR:—*Some physicians give a combination of anterior and posterior pituitary extract by injection for inducing weight reduction. Please let me know whether this is a harmless method.*

M.D., Missouri.

ANSWER.—The use of anterior and/or posterior pituitary extracts for weight reduction is without adequate scientific rationale. Such therapy is apparently a vestige of the tradition that the pituitary gland is responsible for overweight. At present, most authorities accept this view only in rare cases. Control of food intake at the appropriate levels seems to be the main problem in obesity.

TREATMENT OF ERYTHEMA NODOSUM

TO THE EDITOR:—*Is there any new treatment for erythema nodosum?*

Don F. Russell, M.D., Van Wert, Ohio.

ANSWER.—Erythema nodosum is considered to be a symptom complex brought about by any of several causes. It may occur as a toxic or allergic response to drugs, infections, or rheumatic fever. Europeans observe it in association with tuberculosis, particularly in children. Some textbooks state that it may occur as a disease sui generis, usually recurring in the winter months. This type is exceedingly rare. To effect a cure, it is necessary, therefore, to determine the cause. The symptoms usually respond satisfactorily to simple supportive therapy, although cortisone and corticotropin have been successful in giving quick relief from symptoms. If they are employed, they should be used for a short time only.

ARTERIOSCLEROTIC HEART DISEASE IN FIREMEN

TO THE EDITOR:—*Can arteriosclerotic heart disease be considered an occupational hazard under any circumstances? I am particularly interested in knowing whether this is applicable to members of city fire departments and if compensation claims can be made on this basis.*

Howard B. Brown, M.D., Springfield, Mass.

ANSWER.—There is no evidence that either arteriosclerosis or coronary heart disease (an involvement of the coronary arteries with sclerotic changes) is occupational. Aggravation of existing coronary heart disease may be caused by unusual exertion, effort, or excitement. This being the case, the problem is to set up an examination for firemen that will bring to light any evidence of coronary heart disease, and, if this is found, to eliminate afflicted persons from active service as firemen.

RECURRENT JAUNDICE

TO THE EDITOR:—*A patient who received a yellow fever inoculation in May, 1945, contracted jaundice, along with several fellow workers who received the same inoculation at the same time. On July 14, 1951, he had slight jaundice. Did the attack in May, 1945, predispose the patient to further attacks?*

William S. Crawford, M.D., Tulsa, Okla.

ANSWER.—It is possible that the liver, by a previous attack of serum hepatitis, is made more susceptible to the epidemic disease. This was observed in certain work done during World War II. It is also possible that a slightly active hepatitis may continue for many years and become reactivated sufficiently to produce jaundice again.

ANTIBIOTIC THERAPY OR TONSILLECTOMY

TO THE EDITOR:—*Can a diseased tonsil be cured by antibiotic therapy without an operation?*

M.D., Illinois.

ANSWER.—Prior to the advent of antibiotics, there was every justification for resorting to surgery to remove so-called diseased tonsils. The effectiveness of drug therapy in long-standing infections of the middle ear, sinus, bronchi, and lungs points the way for the treatment of diseased tonsils. Intelligent use of the newer drugs in children reduces the number of cases of diseased tonsils, thereby lessening the number of persons requiring surgery; however, there have been failures, in spite of intensive drug therapy. In instances in which drug therapy fails or in persons subject to recurrent infection in spite of effective drugs, tonsillectomy should be performed.

SCARLET FEVER IMMUNIZATION

TO THE EDITOR:—*What is the consensus regarding immunization against scarlet fever in an institution housing infants and small children?*

A. Tarnawski, M.D., Dixon, Ill.

ANSWER.—There is no reliable method for active immunization against streptococcal infections. Scarlet fever toxin used for immunization will prevent the rash of erythrogenic streptococci which are responsible for clinical scarlet fever. At present, the incidence of scarlet fever in this country is at a very low point, and immunization against it is not extensively employed.

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HYDRATION TREATMENT OF ECLAMPSIA

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and

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Although the specific etiology of toxemia of pregnancy has not yet been revealed, the disturbed physiological processes involved in this symptom complex can be treated successfully. It has been shown repeatedly that in toxemia there is a disturbed water metabolism that seems to be closely related to sodium ion retention.¹ This is explained, in part, the excessive weight gain, the edema, and possibly the oliguria so commonly observed in this condition.

The hypertension of toxemia, and probably also the albuminuria, are manifestations of the angiospastic process that affects the arterioles throughout the body, as well as those of the kidney. Arteriolar spasm can be observed in the eyegrounds, and studies of renal hemodynamics have demonstrated that the afferent glomerular arteriole is also involved.² The relationship between these changes and those previously mentioned as related to water retention are probably close, but for purposes of discussion they are more easily treated as separate factors.

For several years at the University of Tennessee and the John Gaston Hospital we have been interested in the hypertensive or angiospastic component of toxemia, and as a result have directed our therapy of eclampsia along these lines. This approach seemed reasonable to us, for of four deaths from eclampsia before January, 1950, three were related directly to intracranial hemorrhage on the basis of hypertension.

In regional nerve block a potent method of controlling hypertension was discovered, and by employing certain techniques to permit continuous administration of the anesthetic agent, blood pressure could be reduced and maintained at more desirable levels. Using, therefore, the modified combined therapy advocated by Dieckmann, along with regional nerve block in indicated cases, a maternal mortality rate of 4% was obtained. Complacent in

our achievement of reducing a mortality rate that at one time stood as high as 26% in the same hospital,³ we failed to appreciate completely the factor of altered water physiology in these cases until our attention was directed to the work of McPhail.⁴

It should be obvious that the edematous toxemic patient who begs for water, with dry tongue and oliguria, is in reality dehydrated. Such is actually the case, for it has been demonstrated that in spite of extracellular edema these patients suffer from cellular dehydration that is relieved only by administration of fluids. Furthermore, Chesley has found that the incidence of toxemia was lowered in a group of patients who had restricted salt and forced fluid intakes.⁵ On the basis of these facts, a revised therapeutic regimen was drawn up, and a series of cases studied between Jan. 15, 1950, and April 15, 1951. It is the purpose of this report to compare this recent group of 50 cases of eclampsia with an earlier group of 100 cases in which the treatment was by the modified combined technique and regional nerve block.

MATERIAL

Between Nov. 1, 1945 and Jan. 15, 1950, a total of 100 patients with eclampsia were treated at the John Gaston Hospital, during a period when there were 13,197 deliveries. Our incidence of eclampsia, therefore, is 0.75%.

Of these 100 patients, 70 were primiparas, further attesting to the well-known fact that eclampsia is a disease principally affecting women in their first pregnancy. Of even greater interest is the large number (40) of patients who had no prenatal care. This is universally the experience in large charity hospitals, where many of the most critically ill patients have never been seen in the prenatal clinic, often being brought in from outlying rural areas

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Read before the Section on Obstetrics and Gynecology at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 13, 1951.

1. Dieckmann, W. J.: *The Toxemias of Pregnancy*, St. Louis, C. V. Mosby Company, 1941.

2. Turner, H. B., and Houck, C. R.: Renal Hemodynamics in the Toxemias of Pregnancy, *Am. J. Obst. & Gynec.* 60: 126, 1950.

3. Green, G. G.: A Seven Year Review of Eclampsia with Special Reference to Treatment with Veratrum Viride, *Am. J. Obst. & Gynec.* 50: 427, 1945.

4. McPhail, F. L.: *The Toxemias of Pregnancy; Treatment Based on a New Concept of the Etiology*, J. A. M. A. 111: 1894 (Nov. 19) 1938.

5. Chesley, L. C., and Annitto, J. E.: A study of Salt Restriction and of Fluid Intake in Prophylaxis Against Pre-eclampsia in Patients with Water Retention, *Am. J. Obst. & Gynec.* 45: 961, 1943.

following a convulsive seizure. The importance of preventive measures is thus emphasized, and the possible etiological role of malnutrition is suggested.

In this group of 100 cases of eclampsia, there were four deaths. Of these, three resulted from intracranial hemorrhage and one from heart failure. Four of the 100 women had had eclampsia previously. Of a total of 107 infants, including 7 sets of twins, 82 babies left the hospital alive and well. Sixteen infants were stillborn, and nine died neonatally.

Treatment in this early group was along accepted lines, employing barbiturates for sedation, intramuscular administration of a 50% solution of magnesium sulfate, and intravenous administration of 20% glucose solution as a diuretic agent. Rarely was more than a total of 2,000 cc. of fluid given within 24 hours by vein or by mouth. Regional nerve block was instituted when the blood pressure was not adequately controlled, or when restlessness or convulsions persisted in spite of conservative therapy. Of the 100 patients, 66 received nerve block in the form of continuous caudal or continuous spinal anesthesia, and no complications, recent or remote, occurred.

The method of delivery was adapted to the individual case, and for the entire group deliveries were by the following methods:

Spontaneous	32
Low forceps.....	38
Mid-forceps	3
Cesarean section.....	19
Scalp traction.....	1
Breech delivery.....	4
Version and extraction.....	2
Dührssen's incisions and low forceps.....	1

Beginning Jan. 15, 1950, a revised therapeutic routine for the care of eclamptic patients was drawn up, embodying previously proved methods of therapy, plus methods to overcome the altered water metabolism as mentioned above. It may be outlined as follows:

The head of the bed should be elevated 18 in. (45.7 cm.), and the patient should be turned every hour until conscious. The carbon dioxide combining power, nonprotein nitrogen, and total and fractional protein levels of the blood should be determined. A hematocrit reading should be made, and the blood typed and cross-matched. An indwelling catheter should be inserted, and fluid intake and output recorded every six hours.

Amobarbital (amytal®) sodium should be given intravenously in doses of 3.75 to 7.5 grains (230 to 500 mg.) for initial sedation. Subsequently phenobarbital sodium in doses of 3 grains (0.2 gm.) should be given intramuscularly every six hours. If other sedation is needed, 4 cc. of a 50% solution of magnesium sulfate may be administered intramuscularly every four hours for a total of six doses.

Every six hours 1,000 cc. of a 5% solution of dextrose in distilled water should be given intravenously by the Murphy method at the rate of 60 drops per minute. Oxygen should be given by a nasal catheter at the rate of 6 liters per minute. Every three hours 100,000 units of penicillin in an aqueous solution may be administered intramuscularly if the patient is comatose or febrile or if the membranes are ruptured. No ergonovine (ergotrate®) maleate, diethylstilbestrol, or ice caps are used during or after delivery. Oxytocin injection (pitocin®) is used at cesarean section.

The blood pressure, pulse, signs of pulmonary edema, and, if present, fetal heart tones and uterine contractions should be determined every 15 to 30 minutes. In severe cases if the blood pressure is not stabilized in four to six hours at levels lower than those present on admission, continuous regional block should

be instituted to reduce the blood pressure and make intracranial hemorrhage and pulmonary edema less likely. Whenever the pulse exceeds 120 without a temperature elevation to account for it, the patient should be digitalized.

When the eclampsia is well controlled, usually less than 48 hours after admission, a vaginal examination is done and plans are made to empty the uterus by the most conservative means. When the patient is rational, a low sodium acid-ash diet is offered, and up to 6,000 cc. daily of plain water by mouth is made available. The intravenous infusions are discontinued as this intake becomes possible.

In this second group of cases, the incidences of such factors as primiparity and lack of prenatal care closely paralleled those reported in the first group. In percentage, the maternal mortality was exactly the same as that of the first group, with two maternal deaths. There were 42 primiparas in this group; 22 women had received no prenatal care, and 3 had had care of questionable adequacy. One woman had had eclampsia previously.*

The rates of infant survival in the second group were as good, or possibly better, than those in the first group. There were three sets of twins among the 53 infants, 44 of whom survived. Six were stillborn, and three died neonatally.

Regional anesthesia was employed in 33 of the 50 cases, but in only 13 cases was continuous anesthesia used to control blood pressure over a period of several hours. Saddle block anesthesia was employed in the majority of cases for delivery. The methods of delivery in the second group were as follows:

Spontaneous	21
Low forceps.....	17
Cesarean section.....	7
Breech delivery.....	4
Mid-forceps	3
Died undelivered.....	1

COMPLICATIONS OF HYDRATION THERAPY

There are two potential pitfalls to be avoided when patients are given large volumes of fluids. These conditions must be especially kept in mind when fluid is administered intravenously. Mengert and Hermes⁶ have reported cases in which pulmonary edema was precipitated by administration of large amounts of fluid by vein. We share fully this concern of overloading an already impaired circulatory system in the eclamptic patient, but among the cases reported here this complication has not been observed.

Circulatory embarrassment is best avoided by slow administration of fluids intravenously, no faster than 60 drops per minute. It is noted, also, that never do we give more than 1,000 cc. of the isotonic glucose solution in any six hour period. Administering more than 4000 cc. per 24 hours has not been attempted, although in certain cases it has appeared theoretically indicated. It should again be stated that intravenous administration of fluids should be discontinued as early as possible. Once conscious, the usual eclamptic patient will satisfy her own fluid requirements without urging.

The second complication of hydration therapy is the so-called "low salt syndrome." We have observed slightly low serum sodium levels in three instances. There has been no frank manifestation clinically of salt depletion, however, and sodium levels have been brought back to normal without difficulty by administration of isotonic sodium chloride solution. Without close laboratory con-

6. Mengert, W. F., and Hermes, R. L.: The Overtreatment of Eclampsia, J. Missouri M. A. 45: 643, 1948.

trol it is entirely possible that excessive and injudicial therapy could result in muscular weakness, lethargy, and coma as a consequence of sodium depletion. We would advocate, therefore, that whenever hydration therapy is undertaken, electrolyte studies be carried out both before and during treatment. A falling plasma sodium level may thus be detected before sodium depletion is manifested clinically.

COMPARISON OF RESULTS

Although we have achieved no downward revision in our gross figures of maternal mortality, observation of the mothers in the second group has impressed us with their lessened morbidity. When an adequate fluid intake is assured, these patients rapidly become lucid and co-operative. Oliguria, which is usually present, is soon overcome, and massive edema subsides within a few days. So-called "dehydration fever" was not seen among these patients, and there was a noticeable decrease in the problem of thick respiratory secretions, so often a troublesome factor in the management of the eclamptic patient.

Gross fetal mortality in the second group was slightly less than that in the first group. We do not wish to lay too much emphasis on this fact because of the discrepancy in the total number of patients. At a future date, when the present series has been enlarged to equal that of the early group, more valid conclusions may be drawn. It is our impression, however, that these more recent babies were, in general, born in better condition than those delivered before institution of the present methods of therapy. This fact we attribute to the improved maternal and fetal physiology and to the decreased maternal requirement for depressant drugs.

SUMMARY AND CONCLUSIONS

Eclampsia represents an altered body physiology affecting primarily the circulatory system, manifested by hypertension and a disturbed water metabolism. A therapeutic regime has been presented which strikes at the principal points of physiological abnormality found in this symptom complex. Comparisons have been drawn between two series of cases, the chief difference of management being the large volumes of fluid given patients in the second group.

Although hydration therapy has not altered maternal mortality, it is believed that morbidity has been lessened and that, in general, patients given adequate amounts of fluid fare better than those who are further dehydrated as a result of therapy. Gross fetal mortality has been slightly lessened, but definite conclusions will not be drawn until the second series can be enlarged to equal the first, which consists of 100 consecutive cases of eclampsia. The complications of hydration therapy have been mentioned, and steps to avoid these pitfalls have been outlined.

We have not lost sight of the fact that prophylaxis through good prenatal care is by far the most effective treatment of toxemia of pregnancy, and we continue to do what we can to encourage this principle. However, we have to accept a large number of eclamptic patients, and this report deals only with the treatment of active cases. In these cases the object is to empty the uterus by the most conservative means at the optimum time, and the foregoing supportive and corrective measures seem to us to be worth-while.

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COMPOUND F USED ORALLY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Ever since the favorable effects of cortisone on rheumatoid arthritis were reported in 1949,¹ search has been made for other substances which might have the same capacity to suppress the disease and which could be produced in greater abundance and at less cost. Of more than 50 steroid compounds tested, some of which have close chemical structural similarity to cortisone, only one, Kendall's Compound F, has corresponding anti-rheumatic properties. Unfortunately this hormone at present is scarcer than cortisone and more expensive to produce.

A hormone with less tendency than cortisone to induce endocrine complications or one with equal liabilities but with more power milligram for milligram to repress inflammatory reactions would have distinct advantages in the practical management of patients with rheumatoid arthritis. It is now generally agreed that the beneficial effects of cortisone are not lasting and that for improvement to be maintained in chronic diseases,

such as rheumatoid arthritis, it is necessary, in most instances, to continue its administration. The maintenance amounts of the hormone needed to uphold adequate degrees of improvement vary directly, in general, with the severity of the disease, and although persons may differ in susceptibility, the incidence and intensity of complicating hormonal side reactions are determined largely by the size of the daily dose employed.² Whereas satisfactory improvement may be sustained for extended periods by uninterrupted oral administration of relatively small maintenance doses of the hormone in

1. Hench, P. S.; Kendall, E. C.; Slocumb, C. H., and Polley, H. F.: The Effect of a Hormone of the Adrenal Cortex (17-Hydroxy-11-Dehydrocorticosterone: Compound E) and of Pituitary Adrenocorticotrophic Hormone on Rheumatoid Arthritis; Preliminary Report, Proc. Staff Meet., Mayo Clin. 24: 181 (April 13) 1949.

2. (a) Boland, E. W., and Headley, N. E.: Management of Rheumatoid Arthritis with Smaller (Maintenance) Doses of Cortisone Acetate, J. A. M. A. 144: 365 (Sept. 30) 1950. (b) Boland, E. W., and Headley, N. E.: Results of Long-Continued Cortisone Arthritis, California Med. 74: 416 (June)

the majority of patients with less severe rheumatoid arthritis, long range results in patients with severe disease are far less impressive. In a recent study satisfactory degrees of improvement were maintained by long-continued (6 to 15 months) cortisone therapy in 92% of the moderate and mild cases of rheumatoid arthritis, in 70% of the moderately severe cases, and in only 47% of the severe cases.³ The chief obstacle to better results with prolonged treatment was the frequent development of objectionable endocrine and metabolic abnormalities. This limitation applied particularly to patients with severe disease whose maintenance requirements were large and in whom effective doses often could not be tolerated because they incited troublesome hormonal complications.

COMPOUND F

Laboratory Observations with Compound F.—Compound F differs chemically from cortisone in only a single structural detail—a hydroxy radical instead of a ketone group is present at the 11th carbon position of the steroid nucleus. There is evidence to suggest that Compound F may be the principal corticoid elaborated by the adrenal gland and that under conditions of stress it may participate more than cortisone in physiological reactions. When corticotropin (ACTH) is administered to man, large quantities of Compound F and only traces of cortisone are recovered from the urine.⁴ Quantitative determinations of urinary corticoids made in patients with hyperfunctioning adrenal cortical tumors give similar findings. The output of Compound F is increased greatly but that of cortisone only slightly when isolated

beef adrenal glands are perfused in vitro with blood enriched with corticotropin.⁵ Isolated adrenal glands are capable of converting a number of perfused steroids to 11-hydroxy compounds, but, although many substances have been added to perfusion media, not one has yielded cortisone.⁶ These facts have led some to conjecture that cortisone is not a true secretion product of the cortex but rather a metabolite of Compound F.⁷

Certain laboratory studies indicate that Compound F is physiologically more active than cortisone.⁸ Ingle⁹ demonstrated that when nonesterified preparations of Compound F and cortisone were given by continuous intravenous or subcutaneous injection to small laboratory animals, the potency of Compound F was twice as great; comparisons were made on the basis of the muscle-work test, assays of liver glycogen, the ability of the compounds to cause regressive changes in the thymus, and adrenal atrophy. Similar estimates based on work tests and glycogenic activity were made by Pabst and co-workers.¹⁰ Compound F is also more effective in stunting embryo growth when the substances are injected into the yolk sacs of 4 day old chick embryos.¹¹ Moreover, hematologic changes from Compound F appear to be more pronounced¹²; in patients with Addison's disease Thorn¹³ has found that twice as much cortisone as Compound F is needed for equivalent eosinopenic response.

Preparations of Compound F.—Two forms of Compound F are available for clinical investigation: the compound in the free form and its acetate ester. Compound F, or 17-hydroxycorticosterone, and hereinafter referred to as free Compound F, is the pure hormone as it may be extracted from adrenal cortical tissue. The small quantities available are now being prepared by two complex processes of biosynthesis: The first process is perfusion of bovine adrenal glands in vitro with media containing Reichstein's Compound S (11-desoxy-17-hydrocorticosterone), a steroid which may be derived from soy beans and which is devoid of anti-inflammatory properties. During perfusion the isolated gland converts the substance to Compound F by placing a hydroxy radical at the 11th carbon position of the steroid nucleus. The second process is extraction from macerated adrenal gland tissue which has been incubated with Reichstein's Compound S. During the process the steroid is 11-hydroxylated to Compound F by the action of adrenal cortical enzymes. Compound F acetate (17-hydroxycorticosterone-21-acetate) is produced by partial chemical synthesis from desoxycholic acid, a similar but more complicated process than that used in the commercial manufacture of cortisone acetate.

Experiences of Others with Compound F in Rheumatoid Arthritis.—Only small quantities of free Compound F and Compound F acetate have been available for clinical investigation, and, heretofore, the amounts have been insufficient to allow comprehensive studies of their therapeutic potency when administered systemically. Hench and his colleagues demonstrated in 1949¹⁴ that free Compound F, like cortisone and corticotropin, had definite antirheumatic activity. They gave 900 mg. of the hormone intramuscularly to one patient over a period of 12 days; during administration the joint manifesta-

3. Boland, E. W.: Prolonged Uninterrupted Cortisone Therapy in Rheumatoid Arthritis, *Brit. M. J.* **2**: 191 (July 28) 1951.

4. Mason, H. L.: Urinary Excretion of Steroids During Administration of ACTH, in *Clinical ACTH Conference Proceedings of the First Meeting*, edited by J. R. Mote, Philadelphia, The Blakiston Company, 1950, p. 168.

5. (a) Jacobsen, R. P., and Pincus, G.: The Chemistry of Adrenal Steroids, *Am. J. Med.* **10**: 531 (May) 1951. (b) Pincus, G.: In *Adrenal Cortex*, in *Transactions of the First Conference*, New York, Josiah Macy, Jr. Foundation, 1949. (c) Hechter, O.: Characterization of Corticosteroids Released from Perfused Cow Adrenals, *Federation Proc.* **9**: 58, 1950.

6. Letters to the Editor: The Bio-Oxygenation of Steroids at C-11, *Arch. Biochem.* **25**: 457 (Feb.) 1950. Pincus.¹⁰

7. Conn, J. W.; Lawrence, H. L., and Fajans, S. S.: Technical Papers: The Probability that Compound F (17-Hydroxycorticosterone) is the Hormone Produced by the Normal Adrenal Cortex, *Science* **113**: 713 (June 22) 1951. Jacobsen and Pincus.¹⁰

8. Ingle, D. J., and Kuizenga, M. H.: The Relative Potency of Some Adrenal Cortical Steroids in the Muscle-Work Test, *Endocrinology* **36**: 218 (March) 1945. Olson, R. E.; Thayer, S. A., and Kopp, L. J.: The Glycogenic Activity of Certain Crystalline Steroids of the Adrenal Cortex When Administered Singly and with Cortical Extract to Fasted, Normal and Adrenalectomized Rats, *ibid.* **35**: 464 (Dec.) 1944.

9. Ingle, D. J.: Personal communication to the authors.

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12. Forsham, P. H.; Thorn, G. W.; Prunty, F. T. G., and Hills, A. G.: Clinical Studies with Pituitary Adrenocorticotropin, *J. Clin. Endocrinol.* **8**: 15 (Jan.) 1948. Thorn, G. W., and others: Clinical and Metabolic Changes in Addison's Disease Following the Administration of Compound E Acetate (11-Dehydro, 17-Hydroxycorticosterone Acetate), *Tr. A. Am. Physicians* **62**: 233, 1949. Thorn, G. W., and Forsham, P. H.: Metabolic Changes in Man Following Adrenal and Hormonal Administration, in *Recent Progr. Hormone Research* **4**: 229, 1949.

13. Thorn, G. W.: Discussion, in the First Clinical ACTH Conference Proceedings of the First Meeting, edited by J. R. Mote, Philadelphia, The Blakiston Company, 1950, p. 176.

14. Hench, P. S.; Kendall, E. C.; Slocumb, C. H., and Polley, H. F.: Effects of Cortisone Acetate and Pituitary ACTH on Rheumatoid Arthritis, Rheumatic Fever and Certain Other Conditions; a Study in Clinical Physiology, *Arch. Int. Med.* **85**: 545 (April) 1950. Polley, H. F., and Mason, H. L.: Rheumatoid Arthritis; Effects of Certain Steroids Other than Cortisone and of Some Adrenal Cortex Extracts, *J. A. M. A.* **143**: 1474 (Aug. 26) 1950. Hench, Kendall, Slocumb, and Polley.¹

tions improved rapidly, the sedimentation rate decreased from 85 to 24 mm. in one hour, and over-all relief was estimated as 60%. Brief accounts of trials with Compound F acetate given systemically in four patients have been recorded. Two of these patients received the drug intramuscularly (dosage consisted of 100 mg. daily for 24 days in one, and 12.5 mg. daily for 11 days in the other); impressions drawn were that the clinical and metabolic effects were probably somewhat less than would have been expected from cortisone acetate.¹⁵ The remaining two patients received the acetate compound orally, and, although details were not given, the improvement was considered comparable to that which results from cortisone acetate in corresponding doses.¹⁶ Recently Hollander¹⁷ reported that intra-articular injections of Compound F acetate are highly effective in suppressing the inflammatory reaction in joints so treated, whereas similar injections of cortisone acetate yield disappointing results.

PRESENT INVESTIGATION

With the preceding considerations in mind, an investigation was made to determine the clinical response of patients with rheumatoid arthritis to orally administered free Compound F and especially to compare its anti-rheumatic properties with those of cortisone acetate.¹⁸ The therapeutic effectiveness of free Compound F was tested in 15 patients as follows: (1) by determining the response of rheumatic manifestations to initial suppressive doses of the hormone in 5 patients and then making comparisons with the known response to cortisone in similar cases; (2) by comparing the maintenance dose requirements for the two hormones in 10 patients.

Comparison of Effects from Free Compound F and Cortisone Acetate with Initial Suppressive Doses Administered Orally.—Previous Experiences with Suppressive Doses of Cortisone Acetate Administered Orally: More than 150 patients with rheumatoid arthritis have been treated with cortisone acetate by us, and the observations from this experience served as standards for comparisons. In these cases a fairly uniform plan of dosage has been followed, consisting of three stages: (1) period of initial large suppressive doses; (2) period of gradual dose reduction; and (3) period of smaller maintenance dose administration.^{2a} Usual dosages for initial suppressive therapy have been as follows: for severe and moderately severe cases, 200 or 150 mg. daily for the first one or two days, followed thereafter by 100 mg. daily; for moderate and mild cases, 100 mg. on the first and subsequent days. The medicament usually has been taken in four divided doses a day (at meal times and at bedtime); better results are obtained with divided doses because the effects from oral administration wear off rapidly, and a single daily dose frequently fails to provide uniform control over a 24 hour period.¹⁹ Daily doses of 100 mg. have been continued until the clinical manifestations were under satisfactory control; the number of days required for this has varied, more or less, with the initial severity of the disease, averaging in severe cases, for example, about 21 days and in moderate cases about 14 days. When satisfactory improvement has been obtained, the dosage then has been reduced gradually in step-like fashion by 12.5 mg. (½ tablet)

at a time and at intervals of every five to seven days. The smallest dosage reached which would uphold an adequate degree of improvement (not complete inactivation of the disease) has been considered as the patient's maintenance dosage. Treatment then has been continued without interruption for extended periods of time, with adjustments in the maintenance dosage being made periodically as changes in disease activity demanded.²⁰

With such initial large doses of the hormone by mouth, improvement often begins within 24 hours, nearly always within 48 hours, and sometimes within 6 to 12 hours. At first the relief is subjective and consists in lessening of articular and muscular aching and stiffness, reduction of joint tenderness and pain on motion, increased functional capacity, and general sense of well-being. Thereafter improvement proceeds day by day with further diminution of symptoms and gradual reduction of reversible objective manifestations, such as joint swelling. Decreases in erythrocyte sedimentation rates may occur quickly, but generally the changes lag behind clinical improvement by several days, and the rates are not always lowered to levels commensurate with the degree of clinical improvement.

Experience with Suppressive Doses of Free Compound F Administered Orally: Large initial amounts of free Compound F were given to five patients, four women and one man, whose ages ranged from 42 to 56 years. Each patient had active rheumatoid arthritis with classical inflammatory changes in multiple peripheral joints, and the duration of the disease varied from seven months to 13 years. The rheumatoid arthritis was graded as severe in one patient, moderately severe in three, and moderate in one; pretreatment erythrocyte sedimentation rates (Westergren method) were 119, 53, 60, 61, and 48 mm., respectively, in one hour.

Each patient was treated as an ambulatory office patient, and during administration of the hormone, analgesics, other medicaments, and physiotherapy were withheld. None of the patients had knowledge of the nature of the medicament being given. Results were appraised from descriptions of subjective improvement, special detailed examinations of the joints performed twice weekly, and from changes in erythrocyte sedimentation rates.

Because supplies of free Compound F were limited, smaller doses were given on the initial day of treatment than would have been employed for cases of comparable severity if the usual dosage schedule for cortisone acetate had been followed exactly. The three patients with moderately severe and the one patient with moderate rheumatoid arthritis received 100 mg. of the hormone on the first day and for several days thereafter. The pa-

15. Perera, G. A.; Ragan, C., and Werner, S. C.: Clinical and Metabolic Study of 17-Hydroxycorticosterone (Kendall Compound F); Comparison with Cortisone, *Proc. Soc. Exper. Biol. & Med.* **77**: 326 (June) 1951.

16. Ward, L. E., and others: Clinical Effects of Cortisone Administered Orally to Patients with Rheumatoid Arthritis, *Proc. Staff Meet., Mayo Clin.* **26**: 361 (Sept. 26) 1951.

17. Hollander, J. L.: The Local Effects of Compound F (Hydrocortisone) Injected into Joints, *Bulletin on Rheumat. Dis.* **2**: 3 (Oct.) 1951.

18. G. D. Searle & Company supplied most of the free Compound F. Merck & Company, Inc., supplied cortisone acetate. Upjohn Company supplied part of the free Compound F.

19. Boland, E. W., and Headley, N. E.: Oral Use of Cortisone Acetate, *J. A. M. A.* **45**: 8 (Jan. 6) 1951.

20. Headley, N. E.

tient with severe disease took 150 mg. daily for two days and 100 mg. per day for another 13 days (Table 1).

The response to free Compound F was prompt and striking in each patient. Symptoms, such as aching and stiffness, began to subside within a few hours following the first dose of the hormone—within 3, 4, 6, 7 and 10 hours in the respective patients. The subsequent progress was extremely rapid in four of the five patients, and in these very marked degrees of over-all improvement (85% or more), as appraised from both objective and subjective criteria, resulted in four, six, six, and eight days. Improvement progressed less rapidly in the patient with severe rheumatoid arthritis, but was graded as marked after 15 days. Reductions in erythrocyte sedimentation rates occurred with remarkable speed and roughly paralleled the degrees of clinical improvement (Table 1).

improvement was graded as very marked (about 90%), and the only residual joint manifestations consisted of slight thickening and tenderness of the right metatarsophalangeal joints and slight tenderness on deep palpation of the right wrist. The patient was no longer fatigued, the appetite was good but not ravenous, and she was happy and energetic, but not euphoric. A weight gain of 7 lb. (3.2 kg.) was recorded. The elevated erythrocyte sedimentation rate was corrected very rapidly; it was reduced from 61 to 29 mm. in 4 days, to 19 mm. in 6 days, and to 11 mm. in 10 days.

The diet was not curtailed at first, but after eight days on a dosage of 100 mg. per day, slight puffiness of the face and moderate edema of the lower part of the legs developed. A salt-poor diet was then instituted, and the dosage of hormone was reduced to 75 mg. daily; the retained fluid disappeared in two days. No other adverse signs ensued, and fasting blood sugar determinations were consistently normal.

CASE 2.—N. L., a woman, 47, had rheumatoid arthritis graded as moderately severe, which involved proximal interphalangeal and metacarpophalangeal joints of both hands and wrists, the

TABLE 1.—Response of Patients with Rheumatoid Arthritis to Initial Suppressive Doses of Free Compound F Administered Orally

Patient	Age (Yr.)	Sex	Disease Duration	Severity	Dosage	Onset of Improvement (Hr. After 1st Divided Dose)	Total Days of Treatment	Degree and Rapidity of Over-All Improvement	Rapidity of Sedimentation Rate Reduction (Mm., Westergren)	Adverse Effects
S. S.	50	F	2 yr.	Moderately severe	100 mg. daily for 7 days; then progressively smaller doses	10	34	Very marked (90%) in 6 days	53 to 10 in 7 days	Slight edema and slight facial mooning
N. L.	47	F	4 yr.	Moderately severe	100 mg. daily for 4 days; then 75 mg. daily for 11 days	4	15	Very marked (85%) in 4 days	60 to 20 in 7 days	None
M. B.	45	F	8 mo.	Moderately severe	100 mg. daily for 8 days; then progressively smaller doses	3	20	Very marked (90%) in 8 days	61 to 11 in 10 days	Slight edema
W. E.	56	F	13 yr.	Severe	150 mg. daily for 2 days; then 100 mg. daily for 13 days	6	15	Marked (75%) in 15 days	119 to 39 in 15 days	None
R. B.	42	M	7 mo.	Moderate	100 mg. daily for 7 days; then progressively smaller doses	7	10	Very marked (90%) in 6 days	48 to 16 in 6 days	None

REPORT OF CASES

CASE 1.—M. B., a woman, 45, had moderately severe rheumatoid arthritis of eight months' duration. The disease had progressed during this period to involve proximal interphalangeal and metacarpophalangeal joints of both hands, both wrists and shoulders, the right elbow, both ankles and knees, and metatarsophalangeal joints bilaterally. Disability was pronounced; the patient experienced considerable difficulty in walking and feeding herself, and she often needed assistance in dressing and combing her hair. General constitutional symptoms were moderate, and a weight loss of 16 lb. (7.3 kg.) had been sustained. Moderate anemia was present, and the erythrocyte sedimentation rate was 61 mm. in one hour (Westergren method). Previous treatment consisted only of salicylates, physiotherapy, and rest.

Free Compound F was given orally in daily amounts of 100 mg. (taken in four divided doses) for eight days; then smaller amounts were given for seven days. The immediate response was rapid and dramatic. Within three hours following the first dose the patient noted less aching, stiffness, and restricted movement in the fingers, wrists, and shoulders. Swelling of the metacarpophalangeal and proximal interphalangeal joints of the hands began to recede after 12 hours, and within 24 hours objective improvement generally was marked. On the second day of therapy she walked almost normally and could perform with ease and little discomfort such acts as feeding herself, dressing, and combing her hair. Progress continued, and on the third day she drove an automobile to the office, being able to grip the steering wheel firmly without pain. After the hormone had been given for eight days in doses of 100 mg. a day, the over-all

right elbow, the left shoulder and sternoclavicular joint, both knees, and metatarsophalangeal joints bilaterally. The disease began insidiously four years previously and, except for temporary improvement following gold salt therapy, had progressed steadily. Chrysotherapy was discontinued 13 months before because of dermatitis. For three months prior to hormonal treatment disability was marked; the patient had difficulty in feeding herself and in gripping objects, was assisted by her husband in bathing and dressing, and walked cautiously with a limp. Her appetite was poor, and she felt weak, tired, and "useless." Moderate hypochromic anemia was present, and the erythrocyte sedimentation rate was 60 mm. in one hour.

Free Compound F was given orally in amounts of 100 mg. a day for four days. Clinical improvement ensued so rapidly that the dose was then reduced to 75 mg. a day for the next 11 days. Four hours following the first dose of the hormone, the patient was aware of less aching and stiffness in various joints, especially those of the fingers. After eight hours both she and her husband noted that swelling and tenderness of the small joints of the fingers were less. Ten hours after beginning treatment she was able to cook dinner energetically and gripped cooking utensils easily. Within 72 hours practically all swelling had disappeared in the metacarpophalangeal and proximal interphalangeal joints of the hands, wrists, and knees, and the left shoulder remained only slightly restricted. By the fifth day objective examination revealed only slight residual tenderness in both wrists with slight swelling of the right, slight thickening and tenderness of the metatarsophalangeal articulations bilaterally, and minimal restriction of motion of the left shoulder. The patient's feeling of fatigue was gone, her appetite was good, and

the general attitude was one of elation and alacrity. Progress continued after the dosage of hormone was reduced to 75 mg. a day. Erythrocyte sedimentation values diminished rapidly—from 60 to 42 mm. in four days and to 20 mm. in seven days. No endocrine complications intervened, and fasting blood sugar determinations made twice weekly remained normal.

Comparisons with Effects from Suppressive Doses of Cortisone Acetate: The number of patients treated with suppressive doses of free Compound F is too small to provide conclusive data, but certain comparisons with cortisone acetate appear justified. The over-all pattern of clinical improvement was much the same with the two preparations, but with free Compound F suppression of the disease took place with greater celerity, and for the short periods of administration involved improvement was more complete. The doses of free Compound F employed on the first day were smaller than those ordinarily used with cortisone acetate, and yet the onset of relief was more consistently rapid. In four of the five

ferring treatment of patients already stabilized on maintenance doses of cortisone acetate to free Compound F and by comparing the dosages required for similar degrees of clinical improvement, it was possible to estimate differences in antirheumatic potency. The maintenance requirements for cortisone acetate were well-established beforehand, since the patients had been treated uninterruptedly for periods ranging from 3 to 16 months. Improvement before transfer to free Compound F administration was graded as marked (70 to 85%) in each case. Thus the rheumatoid arthritis was not fully suppressed; patients were not entirely free of musculoskeletal symptoms, and measurable objective joint findings remained. Patients held under this degree of control are usually sensitive to relatively small alterations of their maintenance dose schedules, and decreases or increases of 10 or 12.5 mg. ($\frac{1}{2}$ tablet) a day are reflected symptomatically. Attempts were made to determine the dosage of free Compound F required to maintain the same de-

TABLE 2.—Comparison of Maintenance Dosage Requirements for Free Compound F and Cortisone Acetate Given Orally in Patients with Rheumatoid Arthritis

Comparative Maintenance Doses for Approximately Equivalent Amounts of Clinical Improvement										Calculated Dosage Ratios (Cortisone Acetate to Free Compound F)*
Patient	Severity of Disease	Degree of Over-all Improvement	First Comparison		Second Comparison		Averages			
			Cortisone Acetate (Mg.)	Free Compound F (Mg.)	Cortisone Acetate (Mg.)	Free Compound F (Mg.)	Cortisone Acetate (Mg.)	Free Compound F (Mg.)		
M. R.....	Moderately severe	Marked (85%)	62.5	40.0	62.5	40.0	62.5	40.0	1.56 to 1	
B. H.....	Moderately severe	Marked (85%)	62.5	40.0	62.5	40.0	62.5	40.0	1.56 to 1	
M. O.....	Moderately severe	Marked (75%)	75.0	50.0	75.0	55.0	75.0	52.5	1.43 to 1	
E. S.....	Moderately severe	Marked (85%)	62.5	40.0			62.5	40.0	1.56 to 1	
M. S.....	Severe	Marked (75%)	75.0	50.0	75.0	50.0	75.0	50.0	1.50 to 1	
L. B.....	Severe	Marked (80%)	125	80.0	125.0	70.0	125.0	75.0	1.70 to 1	
J. S.....	Severe	Marked (75%)	68.8	40.0	62.5	40.0	65.7	40.0	1.64 to 1	
L. E.....	Moderately severe	Marked (85%)	62.5	40.0			62.5	40.0	1.56 to 1	
L. H.....	Moderately severe	Marked (85%)	62.5	40.0	75.0	40.0	68.8	40.0	1.70 to 1	
J. H.....	Moderate	Very marked (90%)	50.0	35.0			50.0	35.0	1.43 to 1	

* Average = 1.56 to 1.

patients objective manifestations of joint swelling, tenderness, local heat, and pain on motion receded very quickly; after four to eight days only minor objective evidences of active joint inflammation remained, and improvement was graded as very marked. Such results do not regularly occur within such short periods from like doses (100 mg. daily) of cortisone. In one patient (W. E., Table 1) with severe arthritis, the rate of disease regression was considered to be about the same as might have taken place with the use of cortisone. Corrections of elevated erythrocyte sedimentation rates occurred more rapidly and coincided more closely with clinical improvement.

These observations led us to believe that free Compound F was probably more effective, milligram for milligram, than cortisone acetate in suppressing the inflammatory changes of rheumatoid arthritis and suggested that smaller amounts of the hormone might be sufficient to bring the disease under initial control. The relative potencies of the two preparations could not be assessed satisfactorily on the basis of immediate response to suppressive therapy in various patients; more accurate appraisals may be made by direct comparisons of maintenance dose requirements in the same patient.

Comparisons of Maintenance Dosage Requirements of Free Compound F and Cortisone Acetate.—By trans-

gree of rheumatic improvement as had been achieved from known daily amounts of cortisone acetate. Once this was established, the result was cross-checked by readministering cortisone acetate in its original dose. Care was taken not to make transfers in rapid sequence, and patients were usually given the test preparation for two to three weeks. In general, changes in the subjective and objective musculoskeletal symptoms were relied on to guide manipulations of dosage more than were modifications in erythrocyte sedimentation rates. Clinical improvement or regression was quickly mirrored by sedimentation rates when free Compound F was being administered, but changes in rates were usually tardy and less decisive with cortisone acetate.

Comparisons of dosage requirements were made in 10 patients, and these demonstrated that free Compound F was consistently more potent in antirheumatic activity than cortisone acetate, when the two substances were administered orally (Table 2). Dosage differences were well-defined and quite uniform; in seven patients comparison studies were performed twice, and the dosage differences during both trials were approximately the same. Dosage ratios of cortisone acetate to free Compound F varied from 1.43: 1 to 1.7: 1 among the 10 patients, and the average ratio for the group was 1.56: 1. These findings indicate that free Compound F is roughly

50% more potent than cortisone acetate and that substantially smaller amounts of free Compound F are needed to maintain similar degrees of improvement in patients with rheumatoid arthritis.

Observations on Adverse Effects.—Since free Compound F was administered for only brief periods, it was not possible to compare the incidence of hormonal complications with those from cortisone acetate. Two patients experienced adverse reactions while receiving initial suppressive doses (100 mg. a day) of free Compound F. Slight puffiness of the face and moderate edema of the lower part of the legs developed in one patient after 8 days of treatment, and slight facial mooning occurred in another after 10 days; these signs disappeared promptly when the dosage of the hormone was lowered.

Observations made while testing maintenance dosage requirements of the two hormones suggested that although free Compound F possessed greater antirheumatic activity than cortisone, its tendency to produce adverse endocrine effects at least was not greater. Each of the 10 patients who were subjects for the comparison study had received cortisone acetate for long periods beforehand, and 5 of them demonstrated signs of cortisone excess. In each of these some or all of the adverse signs disappeared or lessened after transfer to free Compound F administration, and in no instance did new complications arise. In four patients slight to moderate edema was present, which disappeared entirely after transfer. Two patients had definite facial mooning, which became less in one and receded completely in the other. Facial hypertrichosis remained unchanged in one patient. We have assumed that this lessening of adverse effects is accounted for by the fact that after transfer to free Compound F, smaller doses of hormone were used to control the rheumatoid arthritis.

Because studies in adrenalectomized rats indicate that the glycogenic activity of Compound F is substantially greater than that of cortisone²¹ and because massive doses of hormone (400 mg. a day) given to man may reduce the tolerance to carbohydrates,⁷ patients were particularly observed for evidences of disturbed carbohydrate metabolism. Fasting blood sugar determinations and urinalyses were made twice weekly while both suppressive and maintenance doses of free Compound F were being given. Glycosuria was not noted in any case, and blood sugar values did not deviate significantly from pretreatment levels but remained within normal limits. No gastrointestinal symptoms or other nonhormonal pharmacologic reactions resulted from oral administration of the hormone.

COMMENT

The present study indicates that when administered orally to patients with rheumatoid arthritis, free Compound F is approximately 50% more potent in antirheumatic activity than cortisone acetate. It appears also that the greater antirheumatic activity of free Compound F is not accompanied by a correspondingly greater tendency to produce adverse endocrine complications, and the tendency may even be less. At least in several

patients the hormonal side-reactions, which were induced by preceding maintenance doses of cortisone acetate, decreased or disappeared after treatment was changed to smaller but equally effective doses of free Compound F. These observations suggest that free Compound F may prove to be superior to cortisone acetate as a therapeutic agent. The number of cases studied was too small and the periods of administration too short, however, to allow definite conclusions, and decision as to possible therapeutic advantages must await the results of long term treatment studies.

Free Compound F possesses greater antirheumatic activity, milligram for milligram, than any other substance which we have tested thus far. Comparisons of potency have been made with orally administered free cortisone (cortisone, free alcohol) and Compound F acetate.²² By comparing maintenance dosage requirements in six patients with rheumatoid arthritis, it has been found that free Compound F is approximately 50% more effective than free cortisone and that the potencies of free and acetated cortisone are about equal.

Our results with Compound F acetate have varied widely, and dosage differences have not been as clearly defined as with other preparations. In general, its effectiveness has been inferior to both free Compound F and cortisone acetate. Compared with free Compound F, much larger suppressive doses have been needed to incite similar initial response, and maintenance dosage requirements have been considerably greater; in eight subjects tested nearly twice as much Compound F acetate was needed for equivalent rheumatic control. These clinical studies are being continued, and others, designed to determine possible dissimilarities in solubility and absorption between the free and acetated preparations, are being pursued elsewhere. Recent studies indicate that free Compound F is decidedly more soluble than Compound F acetate in a number of media; it is approximately 3 times more soluble in water, 6 times more soluble in synovial fluid, 35 times more soluble in plasma, and 36 times more soluble in serum albumin.²³ The lower solubility of Compound F acetate could substantially lessen the rate and degree of its alimentary absorption and account, at least in part, for its therapeutic inferiority when administered orally.

SUMMARY AND CONCLUSIONS

Free Compound F, or 17-hydroxycorticosterone, was administered orally to 15 patients who had chronic rheumatoid arthritis. The hormone was found to be highly effective in suppressing the activity of the disease and, with short term administration, in maintaining control of the rheumatic manifestations. The pattern of improvement with initial suppressive doses was, in general, similar to that which is observed with cortisone acetate used orally. However, the response to free Compound F was more uniformly rapid, and, even though somewhat smaller suppressive doses were used, clinical improvement proceeded at a faster rate, and elevated erythrocyte sedimentation rates were corrected sooner than with cortisone acetate administration. These observations suggested that free Compound F may be more effective, milligram for milligram, in suppressing rheumatic inflammatory changes and that probably smaller amounts of the hormone would bring the disease under initial control.

21. Ingle,⁹ Pabst, Sheppard, and Kuizenga.¹⁰

22. Merck & Company, Inc., supplied Compound F acetate and Upjohn Company supplied cortisone.

23. Solubility studies were performed at the laboratories of Merck & Company, Inc.

By transferring treatment of patients already stabilized on maintenance doses of cortisone acetate to free Compound F, comparisons of the dosage requirements for similar degrees of clinical improvement were made. Free Compound F was found to be consistently more potent than cortisone acetate in antirheumatic activity. Dosage ratios of cortisone acetate to free Compound F ranged from 1.43:1 to 1.7:1, and the average ratio for the group was 1.56:1; thus the potency of free Compound F was roughly 50% greater.

The greater antirheumatic activity of free Compound F did not appear to be accompanied by a corresponding increase in tendency to produce adverse hormonal effects. In several patients endocrine complications which existed during the administration of larger doses of cortisone acetate disappeared or diminished when treatment was

changed to smaller but equally effective doses of free Compound F.

Comparisons made with cortisone and Compound F acetate administered by mouth have demonstrated that free Compound F possesses greater antirheumatic potency than either of these substances. The effectiveness of free cortisone and the acetate form of cortisone in suppressing inflammatory rheumatic manifestations appears to be about equal.

These observations suggest that free Compound F may prove to be superior to cortisone acetate in the practical management of patients with rheumatoid arthritis. A true evaluation of its possible therapeutic advantages, however, must await the results of long term treatment studies.

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RESISTANCE TO CORTICOTROPIN, CORTISONE, AND FOLIC ACID ANTAGONISTS IN LEUKEMIA.

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The eventual failure of the folic acid antagonists to achieve remissions in patients with acute leukemia has often been pointed out in many clinical reports on these compounds. It was felt that it would be of practical value to ascertain whether this failure was due to the development of resistance of the leukemic cells to these drugs, and if so, whether there existed a cross resistance to corticotropin (ACTH) or cortisone. The lack of cross resistance has already been reported in some patients.¹

In experimental studies in two strains of transplanted mouse leukemia, the development of resistance to the 4-amino antagonists of folic acid has been demonstrated.² One of these strains of leukemic cells is still as sensitive as the parent strain to cortisone,³ 2,6-diaminopurine,⁴ triethylene melamine,⁵ and a weak antagonist of folic acid, 9-methyl-pteroylglutamic ("bremfol") acid.⁵

A series of 16 children were treated with hormones after they had ceased to respond to antifolic acid therapy in order to determine if another remission of the disease was possible. Throughout the paper this group will be referred to as Series A. A series of six children were treated with the folic acid antagonists after they had ceased to show satisfactory response to treatment with corticotropin or cortisone. This group will be referred to as Series B.

All patients in Series A had previously shown remission of their disease during treatment with the 4-amino antagonists of folic acid, and in all but two of the patients (cases 5 and 12), these remissions had been repeated two or more times.⁶ The antifolic therapy was only abandoned when toxic manifestations developed on repeated treatment without sign of a remission. At this time it was apparent in every case that the leukemic process showed evidence of progression in spite of energetic treatment. In Series A the disease process had been known to have been established between 8 to 21 months,

with an average of 12 months, before hormone therapy was started. From one to seven months, with an average of three months, had elapsed from the onset of the first symptom of disease to the start of treatment with one of the folic acid antagonists. The first symptom of the disease was taken to be the presenting symptom that was found to be sufficiently persistent to warrant further investigation, and thence led to the final diagnosis of acute leukemia.

In all patients in Series B a remission of their disease had been obtained from the first course of treatment

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with corticotropin or cortisone, and four patients (cases 1, 3, 4, and 6) had second remissions as a result of hormone treatment.⁷ Four patients (cases 1, 2, 5, and 6) were considered to be resistant to hormone therapy when their therapy was changed to folic acid antagonists. In two patients (cases 3 and 4) a severe Cushing's syndrome

toxicity until the bone marrow was able to regain function.

In Series B cortisone or corticotropin was given as the initial form of treatment. The dosage level of corticotropin was 50-100 mg. per day, and cortisone 50-200 mg. per day. Therapy was continued until a remission was established or until it was apparent the leukemic process was progressing rather than regressing.

During hormone treatment the patients were kept on a low-salt diet with normal protein and caloric requirements. The blood pressure, weight, leukocyte count, and hemoglobin were checked daily, and the blood chemistries, CO₂, chlorides, sodium, potassium, blood sugar, and blood urea nitrogen were determined once or twice weekly as indicated. A careful watch was kept for the onset of potassium deficiency, which manifested itself clinically by abdominal distention and lethargy.

Antibiotics and blood transfusions were used in this group of patients only when it was absolutely essential. Every effort was made to study the effect of the hormones alone.

Hormone therapy was usually stopped as soon as a remission had been firmly established, and the patient was followed in the outpatient clinic with marrow aspirations at least once every two weeks. In two patients (cases 1 and 5) cortisone therapy was continued at home after a remission had been well established.

TREATMENT AFTER RESISTANCE HAD DEVELOPED

Series A patients received cortisone in doses ranging from 100-400 mg. per day, or corticotropin at a level of 50-100 mg. per day. The general regimen was the same as that followed during the initial form of treatment for Series B. Antibiotics and blood transfusions were given whenever there was fever, bleeding, or a low hemoglobin value.

Series B patients were treated with amethopterin, 5 to 10 mg. per day by mouth, in the same way described for the initial therapy for Series A patients. Antibiotics and transfusions were used sparingly. These patients were hospitalized throughout the course of amethopterin treatment.

All patients, with the exception of one (case 6), received an adequate course of therapy with amethopterin,

was induced during the second course of hormone administration. These remissions were of such short duration that it was considered unwise to give further hormone therapy, and the folic acid antagonists were employed.

In Series B the disease process had been known to have been established from five to nine months, with an average of eight months, before the start of antifolic therapy. From three weeks to two months had elapsed from the onset of the first symptom of disease to the start of treatment with corticotropin or cortisone.

INITIAL METHOD OF TREATMENT

In Series A the antifolic treatment used previously was given by the intermittent method.⁶ The antagonist 4-amino-N¹⁰-pteroylglutamic acid (amethopterin) was the drug most commonly used. Treatment was usually started at 5 mg. per day of amethopterin, intramuscularly or by mouth, and continued until a remission or toxicity developed. In the latter instance treatment was resumed as soon as the episode of toxicity was over, providing the bone marrow still showed no sign of a remission. It was sometimes necessary to increase treatment to 10 mg. per day, while other patients only tolerated 2.5 mg. per day. The dose appeared to bear no relationship to the weight or age of the patient. Once a remission was established, therapy was discontinued. The patient was followed in the outpatient clinic, and bone marrow aspirations were performed once every two weeks. Particular importance was placed on the marrow examination, as in this way a relapse could be detected before there were clinical manifestations of the disease. Treatment was started as soon as the percentage of leukemic cells in the marrow was greater than 15 to 20%, and again continued until another remission or toxicity developed. Supportive therapy in the form of antibiotics and blood transfusions was given whenever fever or a moderate decrease in hemoglobin was present. By use of these agents it was often possible to tide a patient over a period of severe

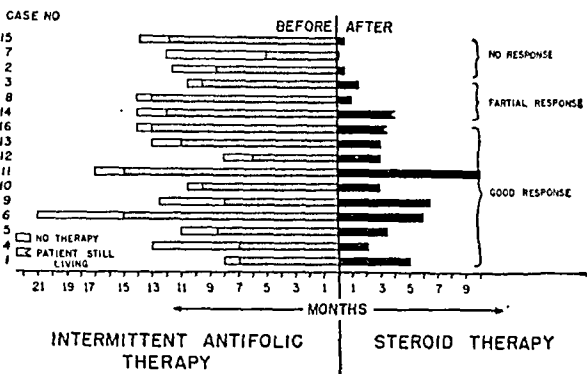


Fig. 1.—Response to corticotropin and cortisone of patients in Series A in whom resistance to amethopterin developed.

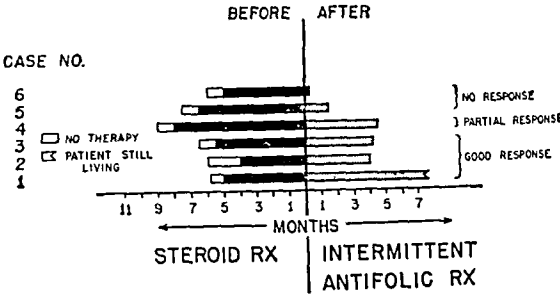


Fig. 2.—Response to amethopterin of patients in Series B in whom resistance to corticotropin or cortisone developed.

based on previous experience with the folic acid antagonists.⁶ This patient had a drop in white blood cell count after four days of treatment, with the onset of bleeding, diarrhea, and mouth ulcerations in another two days. Therapy was discontinued, and the patient died 11 days after amethopterin administration had been started.

7. (a) Pearson et al.; Pearson, O. H.; Eliel, L. P., and Talbot, T. R., Jr.: The Use of ACTH and Cortisone in Neoplastic Disease, *Bull. New York Acad. Med.* 26: 235, 1950. (b) Pearson, O. H., and Eliel, L. P.: Use of Pancreatic Adrenocorticotrophic Hormone (ACTH) and Cortisone in Lymphomas and Leukemias, *J. A. M. A.* 144: 1349 (Dec. 16) 1950.

Cortisone was continued during the first three days of amethopterin treatment.

In our experience, patients treated by the folic acid antagonists usually obtain longer remissions and survive longer. For this reason patients in Series A were given, whenever possible, another course of amethopterin as

intramuscularly administered cortisone (1.05 gm.). Therapy was changed to 5 mg. amethopterin a day by mouth, and after 16 days of this treatment a good clinical and hematological remission was established. Three patients (cases 2, 7, and 15) showed no beneficial response.

Examination of the marrow aspirations in these patients showed an early return of erythropoiesis even while there was still a high percentage of leukemic cells present. This was in contradistinction to the marrow smears of patients on antifolate therapy, where there was first a great decrease in cellularity with a marked fall in leukemic cells in the bone marrow. Later, if a remission was forthcoming, the marrow regenerated and the erythroid cells appeared together with the normal myeloid series.

Seven patients in Series A (cases 1, 4, 5, 6, 11, 13, and 16) were treated with amethopterin as soon as relapse occurred after one course of cortisone or corticotropin. It was hoped that after the course of corticotropin or cortisone, remissions would again be achieved in patients through amethopterin treatment.

Two patients (cases 12 and 14) started amethopterin therapy directly after discontinuing the hormone treatment. One patient (case 9) was tried again on amethopterin after the development of hypertension with petit mal attacks during the second course of corticotropin. In spite of prolonged amethopterin treatment there was no satisfactory response and the patient died. Of the seven patients mentioned above, four patients (cases 4, 5, 6, and 13) have shown no satisfactory response. One patient (case 1) showed some slight evidence of a remission with an improvement in well-being and marrow improvement. This progress was not maintained, and the patient died five months after the cortisone treatment was started, with typical leukemic findings. Two patients (cases 11 and 16, figs. 3 and 4) appear to have regained sensitivity. One patient (case 11) had two eight-week remissions following short courses of amethopterin therapy, and one

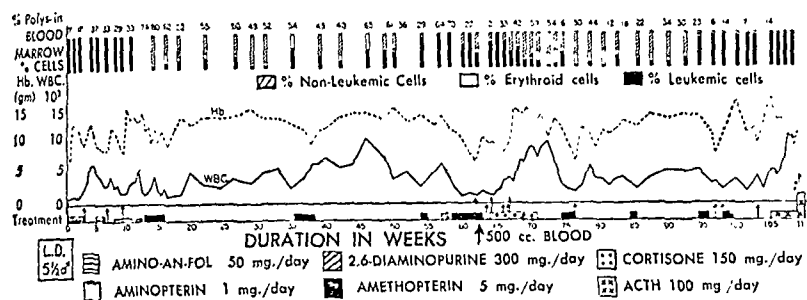


Fig. 3.—Course of disease, laboratory findings, and therapy in patient L. D., male, aged 5½ years.

RESULTS IN SERIES A PATIENTS

A summary of the clinical results and laboratory data are presented in tables 1 and 2. In the patients who responded well to treatment there was an increase in appetite and well-being one and one-half to six days after starting treatment. Diminution of the size of the liver, spleen, and nodes followed later, and marrow improvement was noticed two to five weeks after starting treatment.

The elevation of blood pressure from treatment was sufficient to necessitate discontinuing hormone therapy temporarily in three patients (cases 2, 4, and 6). It is possible that the elevation of blood pressure in two (cases 3 and 8) may have contributed to the immediate cause of death, i. e., cerebral hemorrhage.

The rise in reticulocyte count to over 5% was detected in nine patients (cases 1, 4, 5, 6, 8, 9, 10, 11, and 14), and the drop in the eosinophil counts was demonstrated in eight (cases 1, 4, 5, 8, 10, 11, 13, and 14). A gain in weight was noticed in all patients except one (case 10), and there was often some accompanying pitting edema over the sacrum and lower limbs (cases 2, 3, 4, 6, 8, and 9).

By study of the above criteria, it is seen that 10 patients (cases 1, 4, 5, 6, 9, 10, 11, 12, 13, and 16), had a good clinical and hematological response and three others (cases 3, 8, and 14) showed marked improvement of erythropoiesis in the bone marrow. During treatment two of these three patients (cases 3 and 8) died from an intracranial accident. The other patient (case 14) showed a good improvement in erythropoiesis, but the percentage of leukemic cells in the marrow remained between 60-70% after 32 days of therapy with orally administered cortisone (a total of 9.2 gm.), and seven days of therapy with

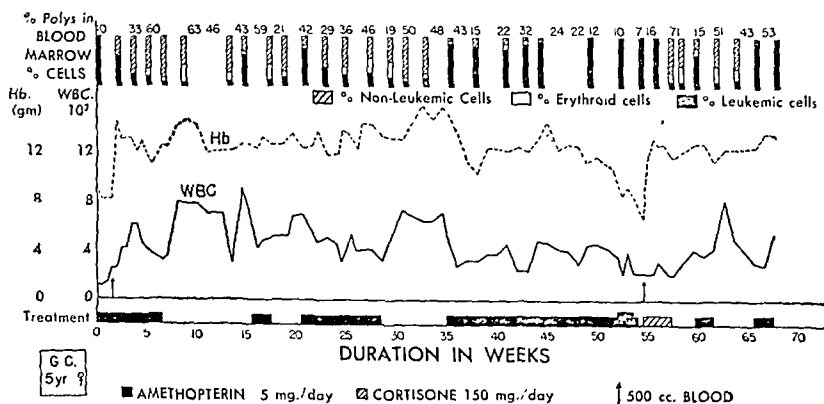


Fig. 4.—Course of disease, laboratory findings, and therapy in patient G. C., female, aged 5 years.

(case 16) has had one remission lasting four weeks, following a course of amethopterin.

The survival time from the start of cortisone or corticotropin therapy to the time of death varied from 3 days to 10 months, and an average for the whole group was 4 months. Two patients (cases 14 and 16) are still living.

TABLE 1.—Therapy and Results in Sixteen Patients in Series A Treated

Case No.	Patient	Age in Yr.	Sex	Time in Mo. from Onset of Disease to Start of Therapy	First Course of Therapy—Folic Acid Antagonists			
					Drug *	Total Dose Mg.	Duration in Days	Results †
1	M. C.....	5	F	1	Ameth.	110	22	R 6 wk
					Ameth.	70	14	T—R 5 wk.
					Ameth.	130	53	T—PR 3 wk.
					Ameth.	100	20	T—NR
2	B. C.....	2	F	2	Anln.	45	21	T
					DAP	8,200	16	T
					Anln.	15	7	T
					Ameth.	85	21	T—R 5 wk.
					Ameth.	187	66	T—R 3 wk.
					A-Ter.	3	6	T
					DAP	1,500	7	T—NR
3	J. C.....	2	F	1	Ameth.	85	7	T
					Ameth.	17	7	R 5 wk.
					Ameth.	215	91	T—R 4 wk.
					Ameth.	70	13	T
					Ameth.	665	30	T
					DAP	2,400	12	T
					Ameth.	15	6	T—NR
4	B. S.....	10	M	6	Ameth.	140	48	T
					Ameth.	85	23	PR 4 wk.
					Ameth.	135	37	T—PR 3 wk.
					Ameth.	40	5	T
5	S. O.....	2	M	3	Ameth.	152.5	50	R 6 wk.
					Ameth.	189.5	143	T
					DAP	1,350	11	T—NR
6	W. K.....	4½	M	6	AAF	1,020	21	T—R 4 wk.
					AAF	650	24	
					Amin.	20	26	R 2 wk.
					Ameth.	110	21	R 3 wk.
					Ameth.	105	20	R 5 wk.
					Ameth.	90	19	R 4 wk.
					Ameth.	95	19	T—R 4 wk.
					Ameth.	135	27	R 5 wk.
					Ameth.	105	22	T
					Ameth.	80	16	T—NR
7	G. B.....	6	M	7	Ameth.	50	19	T—R 4 wk.
					Ameth.	35	7	T
					Ameth.	35	14	R 4 wk.
					Ameth.	22.5	10	T
					Ameth.	20	7	T—NR
8	J. M.....	4	F	1	Anln.	32.5	23	Home
					Ameth.	50	10	T—R 7 wk.
					Ameth.	175	37	T—PR 3 wk.
					Ameth.	220	30	T—R 7 wk.
					Ameth.	145.5	83	T
					Ameth.	100	20	T—NR
9	J. O.....	2¼	M	5	Ameth.	230	57	T—R 9 wk.
					Ameth.	210	65	R 4 wk.
					Ameth.	75	15	T—NR
10	D. Z.....	3½	M	1	Ameth.	75	22	T—R 4 wk.
					Ameth.	85	17	T
					Ameth.	110	21	T
					Ameth.	50	10	T—PR 2 wk.
					Ameth.	155	35	T—R 7 wk.
					Ameth.	35	7	T
					Ameth.	50	10	T—NR
11	L. D.....	5½	M	2	AAF	1,075	21	T
					AAF	600	12	T
					Amin.	20	20	T
					DAP	2,100	20	T
					Ameth.	115	22	R 22 wk.
					Ameth.	85	17	T—R 16 wk.
					Ameth.	35	8	T
					DAP	2,700	.9	T
					Ameth.	72.5	34	T—NR

with Hormones After They Ceased to Respond to Antifolic Acid Therapy

Second Course of Therapy—Hormones		Subsequent Therapy				Total Survival in Mo.
Total Hormone Course **	Results :	Therapy ‡	Dose in Mg.	Duration in Days	Result †	
Cort. 3.75 gm. over 25 days	Liver 8—5 Spleen 10—3 Inguinal and cervical nodes ++ — 0 Reticulocytes 3.6%—9.0% Eosinophils 137.5/cu. mm. to 1.6/cu. mm. Blood Pressure—no change Weight + 1 lb. (0.5 kg.) Remission 3 wk.	Ameth. Ameth.	50 .. 20	10 .. 5	T (Pneumonia) Died	13
ACTH 0.65 gm. over 14 days	Liver 13—8½ Spleen 13½—8 Nodes generalized—no change Reticulocytes 0.6%—10.3% Eosinophils 1.6/cu. mm. to 0 Blood Pressure—initial rise Weight + 5 lb. (2.3 kg.) Died		..	..		12
Cort. 5.55 gm. over 37 days	Liver 8—3 Spleen at costal margin—0 Nodes generalized—0 Reticulocytes 0.2%—2.8% Eosinophils 0—0 Blood Pressure 88/61—150/90 Weight + 1 lb. (1.8 kg.) Died		..	..		12
Cort. 3.5 gm. over 37 days	Liver 5—no change Spleen 8—no change Glands—no adenopathy Reticulocytes 3.1%—8% Eosinophils 14.1/cu. mm. to 10/cu. mm. Blood Pressure 120/85—145/115 Weight + 3½ lb. (1.5 kg.) Remission 3 wk.	Ameth.	20	5	T—Died	13¼
Cort. 3.5 gm. over 34 days	Liver 6—2 Spleen 6—costal margin Nodes generalized—0 Reticulocytes 0.6%—12.6% Eosinophils 6.25/cu. mm. to 0 Blood Pressure—no change Weight + 2 lb. (0.9 kg.) Remission 4 wk. Hypertensive encephalopathy at onset of course	Ameth.	70	33	T—Died	14½
Cort. 7 gm. over 48 days	Liver 4—8 Spleen 4—0 Inguinal nodes +—0 Reticulocytes 0.3%—13.1% Eosinophils 1.6/cu. mm. to 0 Blood Pressure 94/78—110/00 Weight + 9 lb. (4 kg.)	Ameth. Ameth. Ameth. Cort.	62.5 80 15 600	25 16 3 3	T T T Died	27
Cort. 0.2 gm. over 2 days	Died		..	..		12
Cort. 4.2 gm. over 33 days	Liver 9—2 Spleen 9—5 Nodes generalized—0 Reticulocytes 1.1%—5.8% Eosinophils 6.25/cu. mm. to 0 Blood Pressure 110/75—160/110 Weight + 1 lb. (0.5 kg.) Died	Died; Intracranial hemorrhage Marrow—50% erythroid cells				15
ACTH 0.96 gm. over 23 days	Liver 3—costal margin Spleen 12½—costal margin Nodes generalized—0 Reticulocytes 0.1%—10.1% Eosinophils 1.6/cu. mm. to 0 Blood Pressure—no change Weight + 6½ lb. (2.9 kg.) Remission 6 wk.	ACTH Cort. Ameth. Ameth. Ameth. ACTH	700 1,500 165 40 50 200	14 11 30 11 21 4	Hypertension Hypertension T T T—NR Died	19½
Cort. 3.1 gm. over 37 days	Liver 8—4 Spleen 11—4 Nodes generalized—no change Reticulocytes 0.1%—17.6% Eosinophils 42.2/cu. mm. to 0 Blood Pressure—no change Weight 13¼ lb. (0.8 kg.) Remission 5 wk.	Cort.	8,000	20	Died	13½
Cort. 7.4 gm. over 47 days	Liver 3—no change Spleen tip—0 Nodes generalized—0 Reticulocytes 0.3%—8.1% Eosinophils 12.5/cu. mm. to 0 Blood Pressure—no change Weight + 7 lb. (3.2 kg.) Remission 3 wk.	Ameth. Ameth. Ameth. Ameth. ACTH Cort.	70 40 57.5 40.5 2,600 1,200	11 8 11 17 20 3	T—R 8 wk. T—R 9 wk. T T—NR Died	27

TABLE 1.—Therapy and Results in Sixteen Patients in Series A Treated with

Case No.	Patient	Age in Yr.	Sex	Time in Mo. from Onset of Disease to Start of Therapy	First Course of Therapy—Follicle Acid Antagonists			
					Drug *	Total Dose Mg.	Duration in Days	Results †
12	J. T.....	3	M	2	Ameth.	175	47	T
					Ameth.	85	15	R 3 wk.
					Ameth.	480	93	T—NR
13	S. H.....	2	M	3	Ameth.	130	49	R 5 wk.
					Ameth.	125	25	T
					Ameth.	55	14	R 5 wk.
					Ameth.	120	30	R 5 wk.
					Ameth.	80	18	T—R 4 wk.
					Ameth.	70	14	T—R 3 wk.
14	C. T.....	4	F	2	Ameth.	20	9	T—NR
					Ameth.	305	40	R 7 wk.
					Ameth.	115	24	R 5 wk.
					Ameth.	70	14	T
					Ameth.	125	30	T—R 5 wk.
15	J. E.....	10 mo.	M	3	Ameth.	252.5	89	T—NR
					Ameth.	75	28	R 9 wk.
					Ameth.	75	39	R 2 wk.
					Ameth.	175	42	R 3 wk.
					Ameth.	57.5	14	T
16	G. C.....	4½	F	1	Ameth.	280	75	R 5 wk.
					Ameth.	95	20	T—NR
					Ameth.	230	50	R 9 wk.
					Ameth.	130	26	R 3 wk.
					Ameth.	280	57	T—R 3 wk.
					Ameth.	640	126	T—NR

* Ameth. = amethopterin (4-amino-N¹⁰-methyl-pteroylglutamic acid). Anln = aminopterin (4-amino-9-methyl-pteroylglutamic acid). DAP = 2,6-di-aminopurine. AAF = amino-an-fol (4-aminopteroylaspartic acid). Amin. = aminopterin (4-aminopteroylglutamic acid). A-Ter. = aminoteropterin (4-aminopteroyltriglutamic acid).
† R = remission; T = toxicity; PR = partial remission; NR = no remission.

TABLE 2.—Therapy and Results in Six Patients in Series B Treated with Folic Acid

Case No.	Patient	Age in Yr.	Sex	Time in Mo. from Onset of Disease to Start of Therapy	First Course of Therapy—Hormones			
					Hormone *	Total Dose	Duration in Days	Results †
1	P. S.....	3	F	1	Cort.	1.7 gm.	20	R—6 wk.
					Cort.	3.4 gm.	34	PR—6 wk.
					Cort.	1.8 gm.	42 (maintenance)	Cushing's Syndrome
2	C. F.....	7	F	2	ACTH	1.45 gm.	29	R—12 wk.
3	C. W.....	5	M	1	ACTH	1.5 gm.	19	Relapsed on therapy
					ACTH	1.15 gm.	24	R—4 wk.
4	P. M.....	3	F	1	ACTH	3.22 gm.	64	R—6 wk.
					ACTH	0.35 gm.	7	Cushing's Syndrome
					ACTH	1.4 gm.	28	R—4 wk.
					Cort.	1.4 gm.	14	Hypertension
					ACTH	1.7 gm.	23	R—4 wk.
5	B. P.....	4	F	1	Cort.	0.8 gm.	4	Hypertension
					ACTH	1.3 gm.	26	Hypertension
					ACTH	5.1 gm.	46	R—9 wk.
6	M. W.....	3	M	1	Cort.	2.6 gm.	52	Relapsed on therapy
					Cort.	1.4 gm.	63 (maintenance)	R—4 wk.
					Cort.	8.2 gm.	48	Cushing's Syndrome

* Cort. = cortisone. ACTH = corticotropin. † R = remission. PR = partial remission. ** Ameth. = amethopterin. DAP = 2,6-diaminopurine

RESULTS IN SERIES B PATIENTS

In Series B three patients (cases 1, 2, and 3) showed a good response, one patient (case 4) a partial remission, and two (cases 5 and 6) died showing no improvement. Further remissions by amethopterin therapy were only accomplished in one of these three patients (case 1). One patient (case 4) showed a partial hematological remission, with improvement clinically. The bone

marrow, however, remained with about 50% leukemic forms, and, in spite of good erythropoiesis, the hemoglobin value was never built above 10 gm. without the aid of transfusion.
Four patients (cases 1, 2, 3, and 4) showed a good rise in the reticulocyte count while on treatment, and this in turn was reflected by some ability to build hemoglobin by these patients.

Hormones After They Ceased to Respond to Antifolic Acid Therapy—Continued

Second Course of Therapy—Hormones		Subsequent Therapy			Total Survival in Mo.
Total Hormone Course **	Results †	Therapy §	Dose in Mg.	Duration in Days	
Cort. 3.9 gm. over 26 days	Liver 3—no change Spleen 3—0 Generalized small nodes—0 Reticulocytes 0.5%—3.5% Eosinophils 3.1/cu. mm. to 0 Blood Pressure slight elevation Weight + 2 lb. (0.9 kg.) Remission 4 wk.	Ameth.	107.5	35	T—NR
		B ₁₂	6.7	7	
		Cort.	1,650	11	Died
Cort. 2.85 gm. over 19 days	Liver 3—no change Spleen 5—0 Generalized adenopathy—0 Reticulocytes 0.2%—2.9% Eosinophils 32.8/cu. mm. to 0 Blood Pressure—no change Weight + 1 lb. (0.5 kg.) Remission 4 wk.	Ameth.	85	14	T
		Ameth.	10	4	T—NR
		ACTH	1,030	22	
		Ameth.	22.5	5	Died
Cort. 10.25 gm. (9.2 p.o. 1.05 i.m.) over 39 days	Liver 2—at costal margin Spleen at costal margin—0 Generalized adenopathy—0 Reticulocytes 4.2%—3.5% Eosinophils 25/cu. mm. to 0 Blood Pressure—no change Weight + 6 lb. (2.7 kg.) Partial remission	Ameth.	85	17	R 2 wk.
		Ameth. and CF	Under treatment		18+
ACTH 0.48 mg. over 8 days	Liver 2—2 Spleen 0—0 Nodes generalized—no change Reticulocytes—no record Eosinophils—no record Blood Pressure—no change Weight—no change Died		..	..	
Cort. 2.7 gm. over 18 days	Liver 3—no change Spleen 0—no change Nodes 0—0 Reticulocytes 0.3%—1.2% Eosinophils 1.7/cu. mm. to 0 Blood Pressure—no change Weight + 2 lb. (0.9 kg.) Remission 4 wk.	Ameth.	55	11	R 4 wk.
		Ameth.	Under treatment		17+

** Cort. = cortisone; ACTH = corticotropin.
† Liver and spleen are measured in centimeters below costal margin in midclavicular line.
‡ Abbreviations as in * and **, CF = synthetic citrovorum factor (N⁵-formyl-5,6,7,8-tetrahydropteroylglutamic acid).

Antagonists After They Ceased to Show Response to Corticotropin or Cortisone

Second Course of Therapy—Folic Acid Antagonists					Final Course of Therapy			
Drug **	Total Dose in Mg.	Duration in Days	Results		Therapy §	Dose	Duration in Days	Result
			% Reticulocytes	Remission in Wk.†				
Ameth.	55	15	3.9—6.1	4			..	
Ameth.	70	14	0.8—1.0	4				
Ameth.	295	65		2				
Ameth.	105	21		7				
DAP	1,400	17		During R				
Ameth.	125	25		R				
Ameth.	155	46	0.5—5.8	6	Ameth.	At home	..	Died
Ameth.	115	27	1.2—6.3	3	ACTH	2.4 gm.	24	Died
Ameth.	95	21		7 [†]				
Ameth.	75	18		T—NR				
Ameth.	40	5	0.3—0.1	Died			..	
Ameth.	355	64	4.1—12.6	T—PR	ACTH	1.4 gm.	14	Died
Ameth.	120	30	2.5—1.0	T—NR				
Ameth.	230	41		Died			..	

† R = remission, T = toxicity, NR = no remission, PR = partial remission, § Ameth. = amethopterin, ACTH = corticotropin.

The survival time from the start of amethopterin treatment to the time of death varied from 11 days to 6 months, giving an average for this small group of 3 to 4 months.

COMMENT

The development of resistance of bacteria and protozoa to chemotherapy has been demonstrated by many investigators. In somewhat similar studies, the cells of

two strains of transplantable mouse leukemia have been shown to develop resistance in a manner comparable to that of bacteria."

The development of resistance in the 16 patients in Series A was demonstrated by the fact that prior to hormone therapy at least one episode of antifolic toxicity had developed without a subsequent remission. After the usual time had elapsed for the toxicity to clear without a

remission developing 10 of the 16 patients then obtained remissions by a course of corticotropin or of cortisone. Hence it was demonstrated in these patients that there was no cross resistance between the hormone therapy and the folic acid antagonists. That a remission resulted in these patients from hormone treatment would also indicate that they were resistant to the folic antagonist therapy, and not merely so far along in the course of their leukemic disease that they were unable to respond to any form of therapy.

It was hoped that after a course of hormone treatment the leukemic cells would lose their resistance to amethopterin, and further remissions from this form of therapy would be obtained.⁸ The manifestations of toxicity from amethopterin were again demonstrated by the 10 patients so treated following hormone therapy. But only in two of these patients (cases 11 and 16) did remissions develop after their episodes of toxicity. In these patients it is considered that the leukemic cells lost their previous resistance to amethopterin following, or possibly as a result of, hormone therapy.

Metabolic data on one of the patients in Series B has been reported elsewhere (case 2).⁹ The data show that during the second course of corticotropin treatment there was a sharp rise in the urinary excretion of formaldehydogenic steroids and a moderate rise in ketosteroid excretion. These observations indicate that treatment induced an increase in adrenocortical activity, and it is apparent that the failure to obtain a remission was not due to the lack of response of the adrenal cortex, but rather that the leukemic cells had become resistant to the effects of the increased adrenal cortical function.

In other patients in this series, relapse of the leukemia occurred despite evidence of increased adrenal cortical function.

In Series A the average prolongation of life for the whole group was four months, and with two patients (cases 14 and 16) still living at the time of this report it felt worthwhile to continue this method of approach for future patients.

In Series B there was an average prolongation of life from three to four months, but only one patient (case 1) has had repeated remissions from amethopterin treatment. The reason for this is not clear, and in this very small series of cases it is not possible to draw any definite conclusions.

The remissions following either type of treatment are characterized by an improvement in clinical status, a return of the bone marrow to normal function that is in turn reflected in the peripheral blood by a reticulocyte response, an ability to build and maintain hemoglobin, and a normal total and differential white blood cell count. From these facts and other data presented, it would appear that although the remissions resulting from hormone treatment on the one hand, and the folic acid antagonists on the other, develop along similar lines, these drugs probably act through quite different mechanisms.

SUMMARY AND CONCLUSIONS

1. Sixteen children (Series A) with acute leukemia were treated with hormones after no further improvement could be obtained by antifolic therapy.

2. Six children (Series B) with acute leukemia were treated with 4-amino-N¹⁰-pteroylglutamic acid (amethopterin) after no further improvement could be obtained by hormone therapy.

3. Ten patients in Series A had a good clinical and hematological response. One patient had a partial hematological and clinical response. Two patients died during treatment from cerebrovascular accident, but showed significantly increased erythropoiesis in the bone marrow before death. Three patients showed no response.

4. In Series B, three patients had a good clinical and hematological response. One patient had a partial hematological and clinical response. Two patients showed no satisfactory response, and one of these died 11 days after starting amethopterin treatment.

5. The observation that a high percentage of patients respond to hormone or antifolic therapy at a late stage in the course of their disease when they have developed resistance to the other method of therapy suggests that corticotropin (ACTH) and cortisone have a different primary mode of action on the leukemic process from that of the folic acid antagonists.

6. These observations indicate that hormones or folic acid antagonists are effective in producing further remissions in approximately 50% of patients showing resistance to one type of therapy.

7. This method of approach may be of further importance if sensitivity to the original form of treatment can be reestablished.

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9. Pearson and Eliel.^{7b} Pearson, O. H., and Eliel, L. P.: Recent Progress in Hormone Research, Laurentian Conference, 1950, to be published.

Allergy of Urinary Tract.— . . . While urinary tract allergy may occur, the literature contains few reports in which both an organic basis has been completely excluded and an allergic basis incontrovertibly proved by the diagnostic studies which are described. For the skeptic, even the most convincing and suggestive cases are lacking in some important details. In our analysis of 613 patients with six urologic conditions selected because of resemblance to types reported as due to allergy and with etiology either unknown or not fully explained, we find an allergy present in 12% of the group. This percentage is so similar to the accepted incidence of allergy in the general population that we do not feel justified in suspecting that allergy plays any major role in these disorders. In none of our cases who were studied completely urologically and for allergy did the allergy seem to be of etiologic significance. The consensus of clinicians in an unofficial poll is that urinary allergy is very rare.

. . . The urinary tract, in contrast to the skin, respiratory and gastrointestinal tract, has relatively little if any normal contact with foreign protein or other substances in their natural state. It is buffered by the other systems as well as by the blood and lymph, and only those substances which pass this barrier reach the urinary tract. This may be a possible explanation for the infrequency of obvious sensitivity to these agents in the urinary tract and for the difficulty with which we can demonstrate humoral or reagin type sensitivity. Allergy, which involves cellular reactions, would find the kidney no more protected than other body tissues, and we find lesions of this type as frequent or more frequent in the kidney than elsewhere.—Susan C. Dees, M.D., and Eileen C. Simmons, M.D.; Allergy of the Urinary Tract, *Annals of Allergy*, Nov.-Dec., 1951.

EVALUATION OF GYNECOLOGIC SURGERY IN THERAPY OF INFERTILITY

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The clinical data on 500 couples originally examined because of infertility were analyzed by means of an International Business Machine. A study of the subsequent course of these couples showed a decreased incidence of pregnancy in wives who had undergone certain gynecologic operative procedures. The wives with similar pathological gynecologic conditions who did not have operations showed no such decrease, and in some instances had a pregnancy incidence above that of the entire group. A further investigation of the clinical details in the group who had operations and the group who were not operated on was made. In this paper we shall attempt to contrast patients with chronic cervicitis with those who had previous cervical operations, patients with uterine retrodisplacements with those who had had suspensions of the uterus, patients with cystic ovaries with those who had had ovarian operations, and patients with chronic adnexitis with those who had had previous tubal operations.

This group of 500 infertile women had 181 pregnancies following our survey, an incidence of 36.2%. This includes 10 additional pregnancies since our preliminary report,¹ so that necessarily some of the present data will vary slightly from those of the previous report. The overall figures showed that the incidence of pregnancy among the 295 wives who had no pelvic operations prior to our survey (table 1) was 37.9% following our survey. The incidence of pregnancy among 205 wives with a history of previous pelvic operations (290 procedures) was 33.6%. Analysis of the group from another standpoint revealed that, of 205 wives for whom no gynecologic diagnosis was made at the outset of our survey, 88 (42.9%) became pregnant. The remaining 295 wives with diagnoses of pathological gynecologic conditions had a pregnancy incidence of 31.5%. It was interesting also to note that, in contrast to the 290 pelvic procedures performed in 205 wives, urologic procedures (excluding operations in the upper urinary tract) were done in only 39 husbands. In contrasting two groups of patients we correlated certain details, such as history of studies done prior to our survey, presence or absence of dysmenorrhea and dyspareunia, and psychosomatic difficulties. Data from our sterility studies and the general prognoses of the couples in each group were analyzed.

At the termination of the sterility studies, the couples were seen in conference, the results of their studies were reviewed, and estimation of their fertility prognosis was attempted. We graded separately (good, fair, and poor) the prognosis of both the husband and the wife. The outlook for the couple was based on a reasonable combination of the two. The couple's prognosis was decided by the lowest grade assigned to a member, i. e., wife good, husband poor, couple poor. This type of evaluation is justified by the fact that the incidences of pregnancy among persons with each rating were as follows: good, 61.0%; fair, 40.8%; poor, 13.4%.

CERVICAL OPERATIONS AND CHRONIC CERVICITIS

Major cervical operations (cervical amputations, conizations, and extensive cauterizations) had been performed prior to our sterility survey in 49 of the 500 wives (table 2). There were 13 pregnancies in this group, an incidence of 27.5%, less than the incidence of 36.2% for the entire group. Chronic cervicitis was found at the time of our original survey in 110 wives, none of whom had had previous cervical operations. There were 41 pregnancies (37.2%) in this group, 1% more than in the entire group. The remaining 341 wives who had had neither cervical operations nor chronic cervicitis had 127 (37.2%) pregnancies following the survey, also 1% more than the entire group of 500.

TABLE 1.—Comparison of Fertility in Patients with Previous Pelvic Operations and Patients with Gynecologic Abnormalities

	No. Patients	No. Pregnancy	Pregnancy	% Pregnant	Deviation from Total Group Incidence
Total group.....	500	319	181	36.2	
No previous gynecologic operations	295	163	112	37.9	+ 1.7
Previous gynecologic operations	205	136	69	33.6	- 2.6
No gynecologic abnormality..	205	117	88	42.9	+ 6.7
Gynecologic abnormality.....	295	202	93	31.6	- 4.7

TABLE 2.—Comparison of Fertility in Patients with Cervical Operations and Patients with Chronic Cervicitis

	No. Patients	No. Pregnancy	Pregnancy	% Pregnant	Deviation from Total Group Incidence
Cervical operations.....	49	36	13	27.5	- 8.7
Chronic cervicitis.....	110	69	41	37.2	+ 1.0
No operations or cervicitis.....	341	214	127	37.2	+ 1.0
Total group.....	500	319	181	36.2	

In analyzing sterility studies done elsewhere prior to our survey, it was found that women who had had cervical operations also had had more air tubal tests (20% more) and basal metabolic determinations (14% more) than the group as a whole, but no more postcoital examinations. However, the difference was not so marked as might be expected, since in almost all patients the cervical operations were performed to relieve a condition (cervicitis) that a physician considered a factor in the patient's infertility. Certainly a much higher incidence of previous postcoital examinations would have been expected.

The postcoital examination (Hühner) is the most important study in our survey in a comparison of patients with chronic cervicitis and previous cervical operations.

From the Department of Obstetrics and Gynecology and the Division of Endocrinology, Duke University School of Medicine and Duke Hospital. Read before the Section on General Practice at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 14, 1951.

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The number of patients with previous cervical operations who had normal results of postcoital examinations was 13.4% below the 52.2% in the entire group, while the number of patients with chronic cervicitis who had normal findings was only 3% below the figure for the whole group. Further study of the 49 wives who had had

TABLE 3.—Comparison of Incidence of Pelvic Operations in Cervical Operation and Chronic Cervicitis Group

No Pregnancy	Cervical Operations	Suspension Operations	Tubal Operations	Ovarian Operations
Total group (319).....	11.3	7.5	6.0	11.9
Cervical operations (36).....	100.0	...	2.8	8.3
Chronic cervicitis (69).....		4.4	...	4.4
Pregnancy				
Total group (181).....	7.2	6.1	1.7	8.3
Cervical operations (13).....	100.0	...	...	
Chronic cervicitis (41).....		2.4	4.9	2.4

previous cervical operations revealed that 26 still had residual chronic cervicitis (making a total of 136 patients with chronic cervicitis). These 26 patients had 9.9% fewer normal postcoital findings than the entire group, but the 23 patients with previous cervical operations who had no residual cervicitis had 17.4% fewer normal findings. This probably indicates that in these patients the operation was radical enough to eliminate all or most of the cervical glandular tissue.² Among this more radically treated group there were only three (13.1%) pregnancies, while 10 (38.5%) of the 26 patients with cervical operations and residual chronic cervicitis conceived.

A review of the prognoses of the couples was made, comparing the cervical operation group with the chronic cervicitis group. The wives who did not become pregnant in both groups were originally given a better prognosis than the wives of the entire series who did not become pregnant. Among the wives who did become pregnant, the cervical operation group as a whole had been given a better prognosis for pregnancy than the chronic cervicitis group. The latter group had a pregnancy incidence of about average.

TABLE 4.—Comparison of Incidence of Gynecologic Abnormalities in Cervical Operation and Chronic Cervicitis Groups

No Pregnancy	Chronic Cervicitis	Retrodisplacements	Chronic Adnexitis	Cystic Ovaries
Total group (319).....	26.6	21.5	12.9	10.4
Cervical operations (36).....	41.2	19.4	11.2	11.2
Chronic cervicitis (69).....	100.0	21.6	8.6	4.3
Pregnancy				
Total group (181).....	28.2	23.8	2.8	9.9
Cervical operations (13).....	77.0	23.0	7.7	
Chronic cervicitis (41).....	100.0	41.5	2.4	9.8

An analysis of pregnancies that occurred during or after the survey revealed that those wives with previous cervical operations had an incidence of abortion 12.6% above the group incidence of 18.2%. Patients with

chronic cervicitis not treated by surgical means had only 3.7% more abortions than the group as a whole. Both patients who had had cervical operations and patients with chronic cervicitis had had fewer pelvic operations of all types than the 500 wives (table 3), so that other procedures did not influence results.

Pathological gynecologic conditions found during the fertility studies were reviewed. The incidence of these findings among patients with chronic cervicitis was similar to that of the entire group, except for a greater incidence of uterine retrodisplacements (table 4). The same was true for the wives with previous cervical operations, but an increased incidence of chronic adnexitis was found.

SUSPENSION OPERATIONS AND RETRODISPLACEMENT

A history of various types of suspension operations done before our survey was given by 35 patients. Eleven (31.4%) of these patients became pregnant, 4.8% fewer than the 36.2% of the total (table 5). Retrodisplace-

TABLE 5.—Comparison of Fertility in Suspension Operation and Retrodisplacement Group

	No. Pa-tients	No Preg-nancy	Preg-nancy	% Preg-nant	Deviation
Suspension operations.....	35	24	11	31.4	-4.8
Retrodisplacements	104	63	41	39.4	+3.2
No suspensions or retrodisplace-ments	361	232	129	35.8	-0.4
Total group.....	500	319	181	36.2	

TABLE 6.—Comparison of Incidence of Dysmenorrhea Associated with Suspension Operations and Retrodisplacement

	Total Dysmen-orrhea	Moderate Dysmen-orrhea	Severe Dysmen-orrhea	Unknown
Suspension operations (35).....	71.4	45.8	20.0	5.7
Retrodisplacements (104).....	47.0	32.7	14.4	0.9
No suspensions or retrodisplace-ments (361).....	54.5	40.7	11.6	2.2
Total group (500).....	53.8	39.2	12.8	1.8

ments of the uterus were found at the time of our survey in 104 wives. Of these, 41 (39.4%) conceived, 3.2% more than in the entire group.

One would expect that all women subjected to a suspension operation for sterility might at least have had tubal tests, basal metabolic determinations, and/or postcoital examinations.³ We found, however, that 45.8% (4.4% more than in the whole group) of these patients had had tubal tests, 51.4% (12.8% more) had had basal metabolic determinations, and 37.2% (14.2% more) had had postcoital examinations. These figures are not more than 15% above those for the retrodisplacement group.

Is retrodisplacement a cause of dysmenorrhea and/or dyspareunia? Our statistics show that the retrodisplacement group had a smaller incidence of dysmenorrhea than the total group (table 6). The incidence of dysmenorrhea was significantly greater in the group who had had operations. The incidence of dyspareunia was not greater in the retrodisplacement group but was slightly higher in the suspension group (table 7).⁴ Among those who had had suspension operations there were 11.2% more well-adjusted wives than among the retrodisplacement group. There is very little difference between the

2. (a) Meigs, J. V.: The Surgeon Surveys the Sterile Pelvis, *Fertil. & Steril.* 1: 101 (March) 1950. (b) McLane, C. M.: Recent Advances in the Treatment of Infertility, *M. Rec. & Ann.* 43: 718 (Jan.) 1949.
3. Te Linde, R. W.: *Operative Gynecology*, Philadelphia, J. B. Lippincott Company, 1946.
4. Perlin, I. A.: Suspension and the Retroflexed Uterus: Review of Cases, *Am. J. Obst. & Gynec.* 57: 959 (May) 1949.

incidence of well-adjusted wives in the latter group and in the total group.

Retrodisplacement is said to be a factor in tubal occlusion on the basis of congestion, kinks, and associated pathological conditions.⁵ The incidence of conditions associated with tubal occlusion did not vary significantly in the wives who had had suspension operations or retrodisplacement, except that a few more (2.1%) patients who had had suspension operations had closed tubes than those who had retrodisplacement of the uterus. The number of patients who had two or more tubal tests was about the same for the two groups.

The suspension operation is supposed to correct the cervical factor when the cervix is displaced by retroversion. There was no difference in the penetration of sperms among the wives who did not become pregnant in the two groups. In the group who had been treated by operation there was some improvement in the cervical factor in those who become pregnant. There were 10%

TABLE 7.—Comparison of Incidence of Dyspareunia Associated with Suspension Operations and Retrodisplacement

	Total Dyspareunia	Moderate Dyspareunia	Severe Dyspareunia	Unknown
Suspension operations (35).....	20.0	17.2	2.8	0
Retrodisplacements (104).....	13.5	8.6	0	4.9
No suspensions or retrodisplacements (301).....	13.6	8.6	0.5	4.4
Total group (500).....	13.5	8.6	0.6	4.3

TABLE 8.—Comparison of Incidence of Pelvic Operations in Suspension Operation and Retrodisplacement Groups

No Pregnancy	Cervical Operations	Suspension Operations	Tubal Operations	Ovarian Operations
Total group (319).....	11.3	7.5	6.0	11.9
Suspension operations (21)....	4.2	100.0	4.2	28.6
Retrodisplacements (63).....	11.1	...	4.8	20.6
Pregnancy				
Total group (181).....	7.2	6.1	1.7	8.3
Suspension operations (11)....		100.0	...	54.5
Retrodisplacements (41).....	4.9	...	...	4.9

more normal postcoital findings in the suspension group than in the wives of the whole group who became pregnant, while there were 10% fewer in the retrodisplacement group.

Evaluation of the couple prognoses among the wives who remained sterile showed no particular difference between the two groups, except that there were a few (6.6%) more with poor prognoses in the suspension group. The prognosis was good or fair for 14.5% more of the couples in which the wives had suspension of the uterus than for all the couples who had children. The group in which the wives had uterine retrodisplacement had 10.1% fewer good prognoses than all the 500 couples and 9.9% more fair prognoses.

The incidence of abortion is said to be higher in association with retrodisplacement, but this was not confirmed by our statistics. The frequency of abortion was essentially the same in the retrodisplacement group as in the whole group.⁶ There were no abortions in the suspension group. We do not know why, except that there were only 11 pregnancies in the group.

The wives in the suspension group who did not become pregnant had more curettements and ovarian operations and fewer cervical operations than the entire group

(table 8). The women who had retrodisplacement and did not become pregnant had a similar number of cervical operations, fewer curettements, and slightly more ovarian procedures than the 319 wives of the whole group who did not conceive. Comparison among the pregnant wives

TABLE 9.—Comparison of Incidence of Gynecologic Abnormalities in Suspension Operation and Retrodisplacement Groups

	Chronic Cervicitis	Retro- displace- ments	Chronic Adnexitis	Cystic Ovaries
No Pregnancy				
Total group (319).....	26.6	21.5	12.9	10.4
Suspension operations (21)...	12.5	25	20.8	4.1
Retrodisplacements (63).....	28.6	100	11.1	11.1
Pregnancy				
Total group (181).....	28.2	23.8	2.8	9.9
Suspension operations (11)...	9.1	9.1		
Retrodisplacements (41).....	24.1	100	3.2	10.2

shows that there were fewer operations in the retrodisplacement group, but markedly more (38.7%) curettements and ovarian operations (46.2%) in the group with uterine suspension.

Among the wives who did not become pregnant, those with retrodisplacement had approximately the same number of other pathological gynecologic findings as the non-pregnant wives in the entire group (table 9). Among those with normal suspension who remained infertile, slightly more had chronic adnexitis, fewer had chronic cervicitis, and fewer had cystic ovaries. The wives with suspensions who became pregnant had fewer pathological conditions, since the only finding was chronic cervicitis and its incidence was moderately less than in total numbers. Among the patients with retrodisplacement who conceived, there was a higher incidence of endometriosis, chronic cervicitis, and unilateral cystic ovaries.

TUBAL OPERATIONS AND CHRONIC ADNEXITIS

A history of previous fallopian tube operations (unilateral salpingectomy and unilateral and bilateral salpingostomy of various types) was found for 22 of the 500 wives (table 10). Chronic adnexitis (unilateral and bilateral) was diagnosed in 44 at the outset of our survey. The incidence of pregnancy following the survey was 13.6% for both groups.

TABLE 10.—Comparison of Fertility in Tubal Operation and Chronic Adnexitis Groups

	No. Pa- tients	No Preg- nancy	Preg- nancy	% Preg- nant	Deviations
Tubal operations.....	22	19	3	13.6	— 22.6
Chronic adnexitis.....	44	38	6	13.6	— 22.6
No tubal operations or chronic adnexitis	434	262	172	39.6	+ 3.4
Total group.....	500	319	181	36.2	

Previous sterility studies had been done less commonly in both groups except for basal metabolic determinations. The group who had had operations had had 15.8% more basal metabolic determinations than the group as a whole. Dysmenorrhea was present in a few more patients in both groups than in the 500 wives. Dyspareunia, however, occurred much more frequently. The group who had tubal operations had dyspareunia 32% more fre-

5. Ruben, I. C.: Sterility, in Curtis, A. H.: *Obstetrics and Gynecology*, Philadelphia, W. B. Saunders Company, 1933, Vol. 3, pp. 161-214.

6. Barns, H. H. F.: Retrodisplaced Gravid Uterus, *Brit. M. J.* 1: 169-172 (Feb. 1) 1947.

quently than the total. The incidence of moderate and severe dyspareunia was 19% and 13% greater, respectively. Among the group who had not had operations dyspareunia was 25% more frequent; moderate dyspareunia 10%, severe dyspareunia 11%, and data in four cases were unknown. Psychosomatic evaluation of

TABLE 11.—Comparison of Incidence of Pelvic Operations and Gynecologic Abnormalities in Tubal Operation and Chronic Adnexitis Groups

Operations	Cervical Operations	Suspension Operations	Tubal Operations	Ovarian Operations
Tubal operations (22).....	4.5	13.6	100.0	68.2
Chronic adnexitis (44).....	11.3	6.9		4.6
Total group (500).....	9.8	7.0	4.4	10.6

Gynecologic Abnormalities	Chronic Cervicitis	Retro-displacement	Chronic Adnexitis	Cystic Ovaries
Tubal operations (22).....	9.0	13.6	13.6	13.6
Chronic adnexitis (44).....	22.8	20.5	100.0	4.6
Total group (500).....	22.0	20.8	8.8	8.8

the two groups showed a higher incidence of inadequate adjustment in the group who had had operations (28.5% more than in the total of 500).

The hystrogram is the most important single study in the evaluation of these two groups. The groups who had and had not had operations in comparison with the entire group showed, respectively, the following percentage deviations: bilateral patency, —55% and —21%; unilateral patency, +18% and —13%; bilateral closure, +37% and +34%. For the entire survey group unilateral tubal patency was not a detrimental factor,¹ but this certainly was not true when the tube was diseased. Tubal patency may be restored without restoration of tubal motility or ciliary activity. Both subgroups had more repeated tubal tests than the whole group, the group who had had operations having the larger number.

Postcoital examination results for the chronic adnexitis group were about the same as for the total group. There were 15.5% more normal postcoital findings for those who had had tubal operations than for the total group.

The over-all prognosis in both groups was poor but as less favorable in the group with chronic adnexitis. Among the wives who failed to conceive after the survey, the prognosis percentage deviation in comparison with the incidence in the group with operations was as follows:

TABLE 12.—Comparison of Fertility in Ovarian Operation and Cystic Ovary Groups

	No. Patients	No Pregnancies	Pregnancy	% Pregnant	Deviations
Ovarian operations.....	53	38	15	28.3	—7.9
Cystic ovaries.....	44	26	18	41.0	+4.8
No ovarian operations or cystic ovaries.....	403	255	148	36.7	+0.5
Total group.....	500	319	181	36.2	

good, —7.2%; fair, —4.4%; poor, +13.4%. For the group without operation it was good, +3.3%; fair, —22.8%; poor, +18.7%. Among the nine wives in both these groups who did become pregnant, seven had good or fair prognoses.

Many more other operative procedures were done in the tubal operation group than in the chronic adnexitis group (table 11). The operative group had a little higher

percentage of suspensions and a marked increase in the percentage of ovarian operations. The chronic adnexitis group had about the same percentage of suspensions and a slightly smaller percentage of ovarian operations.

The original extent of involvement of the pelvis with infection in the operative group must have been less than that in the nonoperative group, because the percentage of unilateral or bilateral adnexitis varied from survey the average by —2.9% and +6.8%, respectively. The operative group had a slightly higher percentage of retro-displacements and unilateral cystic ovaries than the nonoperative group.

OVARIAN OPERATIONS AND CYSTIC OVARIES

Ovarian operations (simple removal or puncture of a cyst, unilateral oophorectomy, and partial unilateral or bilateral oophorectomy) were done elsewhere prior to our sterility survey in 53 of the 500 wives (table 12). There were 15 (28.3%) pregnancies in this group, 7.9% less than the 36.2% for the whole group. Unilateral or bilateral cystic ovaries were noted at the time of our original pelvic examination in 44 wives. There were 18 (40.9%) pregnancies in these women, 4.7% more

TABLE 13.—Comparison of Incidence of Pelvic Operations and Gynecologic Abnormalities in Ovarian Operation and Cystic Ovary Group

Operations	Cervical Operations	Suspension Operations	Tubal Operations	Ovarian Operations
Ovarian operations (53).....	5.7	24.5	28.3	100.0
Cystic ovary (44).....	6.9			
Total group (500).....	9.8	7.0	4.4	10.6

Gynecologic Abnormalities	Chronic Cervicitis	Retro-displacement	Chronic Adnexitis	Cystic Ovaries
Ovarian operations (53).....	7.6	15.1	9.5	13.3
Cystic ovary (44).....	20.5	29.5	12.9	100.0
Total group (500).....	22.0	20.8	8.8	8.8

than in the entire group. The 403 wives who had neither cystic ovaries nor ovarian operations had 148 (36.8%) pregnancies, 0.6% more than the entire group. More (6.7%) air tubal tests and basal metabolic determinations (12%) were done in women who had operations than in those who did not. Few postcoital tests and almost no endometrial biopsies were performed in either group.

The incidence of dysmenorrhea did not differ significantly in the two groups compared. The incidence of dyspareunia was increased in both groups; the incidence of moderate dyspareunia increased 2.7%, and severe dyspareunia increased 3.7%. In an evaluation of the psychosomatic status it was noted that more (8.6%) patients in the group with operations were considered inadequately adjusted.

The endometrial biopsy was considered important in evaluating these two groups of patients. There was a slightly higher incidence of anovulatory endometria in the group with ovarian operations than among the 500 wives. The cystic ovary group showed no such increase. The incidence of varying degrees of inadequate function of the corpus luteum, as judged by endometrial biopsy, was increased in both groups, but more so among the operative patients.

In both groups couples who had no pregnancies following the sterility studies had as a group about an average prognosis. Comparing the successful couples, the wives who had cystic ovaries had a somewhat better prognosis than those who had had previous ovarian operations. There was higher incidence of pregnancies carried to term in both of these groups than in the 500 wives. There was not a sufficient number of pregnancies in either group to draw any definite conclusions.

Wives with cystic ovaries had fewer operations than the 500 wives (table 13). The ovarian operations group had a marked increase in the incidence of suspensions and tubal operations and a larger incidence of curettages, but they had a smaller incidence of cervical operations than the entire group.

Both groups showed a greater incidence of endometriosis and myomas of the uterus. Among those with previous ovarian operations there was a decreased incidence of chronic cervicitis and retrodisplacements, probably owing to the previously mentioned high incidence of suspensions. The incidence of chronic cervicitis and retrodisplacements of the uterus was considerably greater than the incidence among patients with cystic ovaries, but this appeared to have little effect on the fertility of this group.

COMMENT

The incidence of unnecessary or even function-destroying operations on women is appalling. The reasons for this are well known to most and further discussion is beyond the scope of this paper. It is most illogical to submit a patient to any operation unless one clearly establishes the reason for the operation and critically assays whether it has a reasonable chance of accomplishing its aim. We have been impressed by the casualness with which many of the sterile wives have been operated on.⁷ This is borne out by a comparison of the number of wives and husbands subjected to operations. There were 290 pelvic operative procedures done in 205 wives, and 43 urologic (excluding the upper urinary tract) operations done in 39 husbands. The problems in the two sexes are manifestly different, but this cannot account for all the discrepancy. Of the 500 infertile wives, 41% had pelvic operations prior to our sterility survey. We did operations for the correction of infertility in less than 2% of the wives. Most of these operations were tubal plastic procedures.

Not every operation performed elsewhere was done solely to correct infertility, but we are convinced that the very great majority were. Our sterility practice is largely referral in type. We do not see the infertile couple that has a pregnancy following a cursory examination or the empirical use of thyroid extract, and so forth. Almost all our patients have seen one or more physicians prior to our survey. We have not found that wives who had previous operations (major cervical, suspensions, tubal, or ovarian procedures) were any more adequately studied than those who had no previous operations. This must mean that many of the procedures were done on very questionable indications.

Retrodisplacements of the uterus are frequently considered a cause of dysmenorrhea. Our statistics showed no marked difference in the occurrence of dysmenorrhea

in the retrodisplacement group and among those patients with the uterus in an anterior position. However, there was a markedly higher incidence of dysmenorrhea in the suspension group. Most of these patients probably had dysmenorrhea preoperatively and were led to believe that the suspension would "cure" their dysmenorrhea as well as correct their infertility. The incidence of dysmenorrhea was somewhat higher in the tubal operation and chronic adnexitis groups. This increase was undoubtedly due to the existing pelvic infection. The ovarian operation and cystic ovary groups had approximately the same incidence of dysmenorrhea as the entire group.

The incidence of dyspareunia was not higher in the retrodisplacement group but was slightly higher in the suspension group. Was this due to postoperative changes? The incidence of dyspareunia was markedly higher in both the tubal operation and chronic adnexitis groups. However, it was commoner in the operation group. There was a similar higher incidence of dyspareunia in the ovarian operation and cystic ovary groups. This higher incidence of dyspareunia in both the last two compared groups was probably due to the original pathological condition alone and/or postoperative changes.

Does psychosomatic inadequacy lead to a higher incidence of operative procedures? It seems likely that with many patients it does. However, we found that the average adjustment was slightly better in the suspension group than in either the retrodisplacement group or all the 500 wives. We assume that most of the suspensions were done quite casually on the predicated basis of the widespread (and incorrect) belief that retrodisplacement of the uterus is a common cause of infertility. The tubal operation group had an increased incidence of inadequate adjustment. The anticipated incidence of pregnancy in this group was low, and it was likely that many of these patients could not accept this and were willing and often themselves urged that something be done. For many of these patients conservatism would have been better medical judgment. The ovarian operation group also had an increased incidence of inadequate adjustment. Cystic ovaries in women in the childbearing epoch are usually physiological, unless they persist and increase in size over a period of months.⁸ Our data show that cystic ovaries are not associated with a higher incidence of infertility. The ovarian operations must have been performed on the grounds that they were the cause of infertility. In some patients operations probably were done because the patient who was tense would not wait for a physiological decrease in the size of her ovaries. We are not considering the so-called "white pale" ovaries of the Stein-Leventhal syndrome⁹ which are found in patients with infrequent or absent menses.

The general consensus of opinion over the years has been that sterile wives with chronic cervicitis should at least have a cauterization of the cervix, if not more radical procedures, such as conization and partial amputation of the cervix. It was interesting to discover that the incidence

7. Meigs,^{2a} Te Linde.³

8. Miller, N. F.: The Abuse of Pelvic Surgery in the Female, South. Surgeon 13:821-830 (Nov.) 1947.

9. Stein, I. F.; Cohen, M. R., and Elson, R.: Results of Bilateral Ovarian Wedge Resection in 47 Cases of Sterility: 20-Year End Results; 75 Cases of Bilateral Polycystic Ovaries, Am. J. Obst. & Gynec. 58: 267-274 (Aug.) 1949.

of pregnancy among our sterile wives was considerably less among patients who had cervical operative procedures than among those who had chronic cervicitis (27.5% and 37.2%, respectively). In a study of the results of postcoital examinations (the factor one would supposedly correct with this procedure), we found that there was a higher incidence of abnormal findings in the operative group. There were still 26 patients with residual cervicitis in the operative group, and a comparison of these with the 23 operative patients who had no chronic cervicitis was most revealing. The operative patients with residual cervicitis had a higher incidence of normal findings on postcoital tests and many more pregnancies than the operative patients with no residual cervicitis. This forces us to consider that an operation which is sufficiently radical to eradicate completely chronic cervicitis may also be sufficiently radical to destroy the normal glandular function of the cervix.

Removal of a portion of the cervix (by conization or partial amputation) probably was a factor in the high incidence of abortion in this group of patients. The lower incidence of pregnancy in the cervical operation group was not due to less fertile husbands, since the group had a better prognosis rating than the whole group. Both patients with previous cervical operations and those with chronic cervicitis had a minimum of other pelvic operations and initial pathological conditions.

What do we do for patients with chronic cervicitis when there are abnormal postcoital findings? Formerly, routine use of acid douches was recommended, and an occasional light cauterization was done. Now we treat most patients quite successfully with antibiotics,¹⁰ which change a purulent discharge to a nonpurulent one. We also use small (0.1 mg. daily) doses of diethylstilbestrol, which increase the amount and decrease the viscosity of the cervical mucus.⁹

Thirty-five of the sterile wives who consulted us had had suspension operations done elsewhere prior to our survey. Most of these so-called therapeutic suspensions, done to relieve infertility, are performed with no previous sterility studies on either husband or wife. Some type of suspension operation is performed with the idea that changing the position of the uterus will lead to pregnancy. This assumption is contradicted by the statistics on our group of sterile wives.¹¹ There was a higher incidence of pregnancy in patients with uterine retrodisplacement than in patients with suspension operations (39.4% and 31.4%, respectively).

It is argued frequently, as justification for suspension procedures, that retrodisplacements increase the degree of tubal abnormality and that suspensions, by relieving congestion and kinks, will correct this. There was a slightly greater number of patients in the suspension group with closed tubes. Otherwise, there was very little difference between the results of tubal studies of patients with retrodisplacements and those with suspensions. We did not find the marked improvement in tubal status we would expect if the preceding thesis were correct.

Abnormal postcoital findings have been commonly associated with retrodisplacement of the uterus. Suspension is said to correct the cervical factor. No difference was found between the retrodisplacement and the suspension patients who failed to conceive. Among the patients who became pregnant, the retrodisplacement group had a higher incidence of abnormal findings and the suspension group a higher incidence of normal findings on postcoital tests. Regardless of this discrepancy, there was no difference in the incidence of pregnancy among the retrodisplacement patients. According to our data, the suspension operation may correct abnormal postcoital findings in some patients, but we have not found that this necessarily leads to an increased incidence of pregnancy.

Despite a poorer prognosis rating as a group, the retrodisplacement patients had a higher incidence of pregnancy. All the pregnancies in the suspension operation group occurred in couples with good and fair prognosis ratings, a rather select group of patients. The pregnancy results were good in this group of 11 patients (no abortions). The abortion incidence (19.9%) among the retrodisplacement patients was not significantly above the survey average (18.2%). From a perusal of the literature on retrodisplacements of the uterus, we would expect the abortion rate of our retrodisplacement group to be significantly higher than we found.

The retrodisplacement group did have a much higher incidence of chronic cervicitis and unilateral and bilateral cystic ovaries than did the suspension group. It has been believed that these were serious concomitants of retrodisplacements of the uterus produced by poor drainage and congestion. This may be true, but certainly the fertility of this group was better than of the entire group or the suspension group. The incidence of gynecologic symptoms, such as dysmenorrhea and dyspareunia, was not above average, while these complaints were commoner in the suspension group.

The suspension patients had been subjected to many other operations, usually some ovarian procedure. With the frequent finding of small physiological cysts, the surgeon too often persuaded himself that it was advisable to resect or remove the ovary. It seems apparent that in the infertile patient there is seldom justification for the suspension operation because it does not increase the incidence of pregnancy, does not improve tubal abnormalities, and may lead to a higher incidence of dysmenorrhea and dyspareunia.

The wives who had had previous tubal operations (unilateral salpingectomy and an occasional plastic procedure) and those with chronic adnexitis had a uniformly low incidence of pregnancy. The results obtained on hysterograms explained this. Bilateral tubal closure was found in 50% of the patients in both groups on final tubal tests (group incidence is 10.2%). The operative group had a higher incidence of unilateral patency than did those patients with chronic adnexitis, unilateral or bilateral, probably due to the fact that one tube was removed. Despite tubal patency in some of these patients, the remaining tube or tubes were evidently diseased sufficiently to make pregnancy unlikely. The prognosis rating was poor for both groups, but was poorer in the chronic adnexitis group, although there was a similar incidence of pregnancy.

10. Stein, I. F., and Kaye, B. M.: Symposium on Gynecology and Obstetrics: Newer Methods in the Treatment of the Abnormal Cervix, *S. Clin. North America* 30:259 (Feb.) 1950.

11. Atlee, H. B.: Anteversion of the Retroverted Uterus, correspondence, *Am. J. Obst. & Gynec.* 53:896 (May) 1947.

The tubal operation group had many concomitant ovarian operations, as one might expect. It is difficult to remove a fallopian tube without some embarrassment of the ovarian blood supply, particularly in the presence of chronic pelvic inflammatory disease. A few more suspensions were done in this group. However, the initial pathological condition in these operative patients revealed more retrodisplacements and cystic ovaries than among the patients with adnexal disease.

In viewing both groups of patients, the presence of chronic adnexitis or a history of tubal operations of any type indicates a poor prognosis for infertile patients. It is doubtful if the use of plastic tubal procedures would have a very successful result in either group of patients due to the already existing tubal abnormality which has destroyed the motility and ciliary action of the tube. These data indicate that tubal plastic procedures should not be attempted by one who operates only occasionally.

In comparing the patients with a history of previous ovarian operations and those who initially had unilateral or bilateral cystic ovaries, we again found that the operative patients had a lower incidence of pregnancy (28.3%). The nonoperative group had an incidence of 40.9%, 4.7% more than the group incidence.

An evaluation of ovarian function by means of endometrial biopsy revealed both groups to have a lower incidence of normal ovarian function than the 500 wives, but this decreased incidence was more marked in the operative group. In certain patients bilateral cystic ovaries may lead to a decrease in fertility (Stein-Leventhal syndrome), but most of the operations were done in our patients for the removal of small physiological cysts, which do not interfere with fertility. The removal of these cysts, and in some patients the entire ovary, often results in sufficient change in ovarian blood supply or post-operative scarring to lessen the functional ability of the involved ovary or ovaries. Miller⁸ has shown that 97% of cystic ovaries below 5 cm. in size are physiological cysts. If one observes these patients over a period of time, these small cysts usually disappear. Certainly the presence of such small cystic ovaries did not decrease the fertility of the nonoperative patients. On the basis of our data, a meddlesome ovarian operation does not increase the fertility of the patient.

Reviewing the other operative procedures of both groups, we discovered that those patients with ovarian operations had a higher incidence of other pelvic operations, particularly suspensions and tubal procedures, which undoubtedly had something to do with the poorer pregnancy results obtained. The incidence of initial pathological gynecologic findings was higher in the cystic ovary group, since ovarian cysts, retrodisplacements, and chronic cervicitis commonly occur together. This higher incidence of pelvic abnormalities apparently did not decrease the fertility of this group.

It is quite apparent that a great many infertile women are casually subjected to various operative procedures supposedly to relieve their infertility. Among most couples neither the wife nor the husband has been adequately studied to determine the cause or causes of the infertility. Most of these operations do not accomplish what the physician thinks they will. We have consistently

shown that there was a higher incidence of pregnancy among patients who had initial gynecologic abnormalities similar to that for which these operations are commonly done. Conservatism has been preached by many, but when will it be universally practiced?

SUMMARY AND CONCLUSIONS

In a group of 500 infertile wives a comparison is made of those with gynecologic abnormalities and those who had had operations designed to correct these abnormalities. We have considered sterility studies done prior to our survey, dysmenorrhea, dyspareunia, psychosomatic difficulties, couple prognosis, pertinent data from our survey, and pregnancy results. The compared groups were patients with major cervical operations and those with chronic cervicitis, patients with suspension operations and those with retrodisplacements of the uterus, patients with tubal operations and those with chronic adnexitis, and patients with ovarian operations and those with cystic ovaries. The pregnancy incidence among the 500 wives was 36.2%

There were 110 wives with chronic cervicitis—pregnancy incidence, 37.2%—and 49 with major cervical operations—pregnancy incidence, 27.5%. There was a higher percentage of abnormal postcoital findings (Hühner postcoital test) and abortions in the operative group. The operative patients with residual cervicitis had more normal postcoital findings and many more pregnancies than the operative patients with no residual cervicitis.

There were 104 wives with retrodisplacement of the uterus—pregnancy incidence, 39.4%. There were 35 wives with suspension operations—pregnancy incidence, 31.4%. There was a higher incidence of dysmenorrhea and dyspareunia but a lower one of psychosomatic inadequacy in the operative group, and the incidence of tubal occlusion and normal postcoital findings was slightly higher. Better over-all couple prognosis, a higher incidence of previous operations other than suspensions, and a lower incidence of chronic cervicitis and cystic ovaries were noted in the operative group as compared with the nonoperative group.

There were 44 wives with chronic adnexitis—pregnancy incidence, 13.6%. There were 22 wives with previous fallopian tube operations—pregnancy incidence, 13.6%. Both groups showed a higher incidence of dysmenorrhea, dyspareunia, and inadequate adjustment than the total group. Fifty per cent of each group had bilateral tubal occlusion. The over-all couple prognosis was poor in both groups. The operative group had a high incidence of concomitant ovarian operations.

There were 44 wives with unilateral or bilateral cystic ovaries—pregnancy incidence, 40.9%. Fifty-three wives had had ovarian operations—pregnancy incidence, 28.3%. In both groups the incidence of dysmenorrhea was the same as for the 500 wives and that of dyspareunia higher; inadequate adjustment was commoner in the operative group. Ovarian function was below normal in both groups, but more so in the operative group. Concomitant tubal operations and suspensions were common in the operative group. Retrodisplacement and chronic cervicitis were associated frequently in the non-operative group.

Various pelvic operations (major cervical, suspension, tubal, and ovarian procedures) are associated with a reduced incidence of pregnancy. These operations are done usually without adequate study of the couple. Gynecologic abnormalities (excluding chronic adnexitis) for which these procedures are performed are not

a major cause of infertility. A much more critical attitude toward operation on sterile wives is greatly needed. Tubal plastic procedures should be done only in wives who, with their husbands, have been carefully screened by one well versed in the special techniques.

Duke Hospital (Dr. Carter).

PLEURODYNIA IN CHILDREN

CLINICAL OBSERVATIONS IN FIFTY-FOUR CASES

Samuel J. Nichamin, M.D., Detroit

It has been stated¹ that, in areas where the Coxsackie viruses have become disseminated, as many as 80% of the population may have various mild infections, many of them unrecognized and subclinical. Most of these illnesses occur in children. The symptoms are, for the most part, vague and undifferentiated, assuming an influenza-like character at times, often with an unexplained fever of short duration. They are frequently responsible for the development of various clinical aspects of pleurodynia, or "aseptic meningitis." By its close association with poliomyelitis, especially of the nonparalytic type, pleurodynia has become the most prominent of the various factors related to the many unsolved etiologic problems of this baffling disease.

In order to delineate more clearly one of the above-mentioned clinical syndromes associated with the Coxsackie viruses, some specific aspects of pleurodynia are described as observed in a group of children in private practice. In a previous report² I stressed certain epidemiological and clinical aspects of the disease. My attention has since been directed to its clinical manifestations in childhood. During a period of six years, as I became increasingly aware of the ubiquitous nature of the disease, it became evident that certain illnesses in children previously ascribed to an undefined "viral" etiology could be more accurately designated as pleurodynia.

When there is an explosive outbreak with specific and distinctive symptomatology, the diagnosis of epidemic pleurodynia is easily made, and it is this form of the disease that has been described in the literature. My observations reported here tend to provide a broader concept of this disease, embracing other than its purely epidemic phases.

During the past few years some children who had had an attack of pleurodynia became ill again after intervals of several months or more, with a clinical picture that closely paralleled the initial illness. These illnesses were accordingly designated as recurrent attacks of pleurodynia. Since this was an atypical manifestation for an epidemic disease, an effort was made to compile records of additional cases as further examples. A total of 17 such cases were collected from among my private patients. No

mention of the recurrent aspect of the disease has thus far been recorded. Recognition and correct diagnosis of attacks of this type could possibly lead to identification of some of the vague illnesses of childhood that have been grouped with the Coxsackie virus infections. Laboratory and clinical evidence confirming the causal relationship between the Coxsackie virus and pleurodynia have been steadily accumulating.

Despite the mildness of the disease in most instances, the type and persistence of the complaints often create anxieties in the parents. Symptoms such as headaches, abdominal pains, fatigability, and, occasionally, pain or stiffness about the neck suggest diseases that are the scourge of childhood. The importance of an accurate explanation of these illnesses as representing a specifically named clinical entity with a benign prognosis can be readily understood. However, the physician's diagnostic acumen is often challenged by the close similarity of the symptoms to those of more serious diseases. Skillful assessment of the history and physical findings together with a constant awareness of and familiarity with the widespread incidence of pleurodynia are of the utmost importance.

Various clinical features of pleurodynia as it occurs in children need to be evaluated distinctively. Understandably, a younger child has more difficulty describing and localizing pain or discomfort than an older person. Children under 5 years of age seldom complain of headache. In this age group abdominal pain seems to take precedence over many other types of discomfort. Fatigability can be ascertained more certainly from a history of the patient's behavior. Children of the same age group may vary widely in their ability to describe their symptoms. One must also take into account the fact that pain sensitivity varies more in children than in adults. Pleurodynia in adults characteristically has a more abrupt onset than in children. Fever is not always present. In a significant number of older children headache seems to be the predominant complaint. The history frequently reveals the presence of vague abdominal pain or discomfort over an indefinite period of days or weeks, entirely unrelated to any function. The younger the child the more likely will the pain be referred to the periumbilical region. In childhood one is seldom confronted with the lower thoracic or upper abdominal pain so characteristic of pleurodynia in adults. The quality or intensity of the pain is also less

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1. Coxsackie Viruses, editorial, *Ann. Int. Med.* 34: 257 (Jan.) 1951.

2. Nichamin, S. J.: Clinical and Epidemiologic Aspects of Epidemic Pleurodynia, *J. A. M. A.* 129: 600 (Oct. 27) 1945.

dramatic. Substernal "smothering" sensations are rarely described by children. Only occasionally will a child complain of difficulty or pain in taking a deep breath. Nausea or vomiting have not been prominent symptoms, except in certain instances in which persistent, intractable vomiting prevails. Parents are especially perturbed about the languor, fatigability, and general malaise of the child. Because of involvement of one or both trapezium muscles, in a number of younger patients the pain was referred to the corresponding ears or mastoids. Worried parents brought the children in for examination of these organs, apparently unaware of the presence of other less important symptoms. The absence of pathological conditions in the ears and the finding of tenderness in the muscles of the subcostal regions of the abdomen as well as in the trapezii led to the diagnosis of pleurodynia. On the whole, the condition is not disabling enough to confine the child to bed, though full activity leads to quick exhaustion. Parents are thus inclined to overlook early symptoms of the syndrome.

In view of such a bizarre group of symptoms the examining physician must eliminate at the outset the presence of acute appendicitis or other acute intra-abdominal conditions, as well as poliomyelitis and other central nervous system disease. Painsstaking efforts to discover tenderness in the epigastrium or in either of the subcostal regions will often provide a clue to a definite diagnosis of pleurodynia.

RECURRENT ATTACKS

The times of initial and recurrent attacks of pleurodynia in 17 cases are shown in the accompanying chart, with the number of recurrences indicated for each case. The number of attacks in each quarter during the years of the study are plotted, showing the frequency of attacks in different seasons. Although there is a tendency toward grouping of attacks of pleurodynia within certain quarters and years, cases occurred throughout the period of the study. There is a fairly high concentration of attacks in the third quarter of 1949, with 10 initial and 2 recurrent attacks in this period. Except for two attacks (one initial and one recurrent) in the second quarter of 1950, the recurrent attacks are fairly equally distributed, averaging four to five, for the other quarters of 1950 and the first half of 1951. These findings illustrate first, a definite tendency toward epidemic occurrence of pleurodynia, as evidenced by the high incidence of attacks of the disease during the summer of 1949; and, second, an equal tendency for cases to occur sporadically during other periods of the year.

The frequency of recurrent attacks of pleurodynia is also shown in the chart. In nine cases (53%) there was only one recurrence, but in the remaining eight (47%) there were at least two recurrences. In five cases (29%) the disease was manifested in three or more attacks.

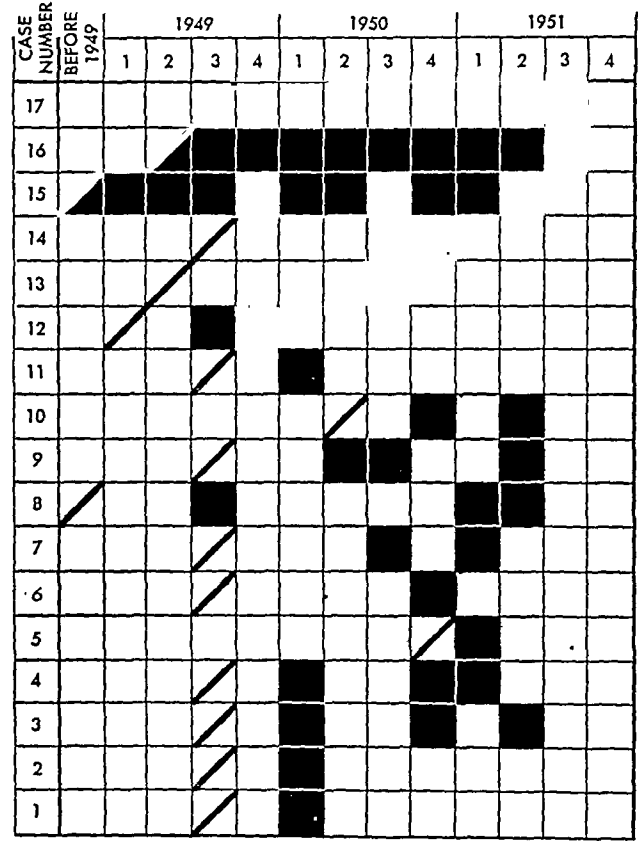
The intervals between the initial and first recurrent attacks of pleurodynia and between the first recurrence and subsequent recurrences were wide and irregular (see the accompanying chart). The periods between attacks ranged from 2 to 30 months. Such an irregular occurrence of repeated attacks seems to preclude considera-

tion of any one constant factor as responsible for precipitating clinical manifestations.

There seemed to be little relationship between seasons of the year and recurrences of pleurodynia, since 14 attacks were observed in the warm months and 16 in the cold months. Weather, of itself, would therefore appear to be less significant in this series of cases than in the epidemic group of cases previously reported.²

No significant predominance of either sex was noted in this group of cases with recurrences. Among the patients who had repeated attacks were 10 boys and 7 girls.

The disease recurred in the younger as well as in the older children; three patients were less than 4 years old, the youngest child being 3 years and 6 months old. How-



Initial and recurrent attacks of pleurodynia in 17 cases according to time of occurrence. Each square with a diagonal line represents an initial attack and each black square represents one recurrent attack. The years are divided into quarters as follows: 1 represents the period from January through March, 2 from April through June, 3 from July through September, and 4 from October through December.

ever, the incidence was greater among children between 5 and 10 years old, with a total of 11 repeated attacks occurring in this age group. Of these, six were between 5 and 7 and five were between 8 and 10 years old. Three children were 11 or older.

TREATMENT WITH AUREOMYCIN

From the long-range, academic viewpoint, there appears to be little incentive to provide effective or specific therapy for a benign self-limited disease like pleurodynia, the etiology of which has been obscure until recently. Since it rarely results in complications and frequently lasts less than a week, one would be inclined to provide

some form of symptomatic treatment, with reassurance to the patient of an early and favorable termination of the disease. Although children show a fairly wide gradation in severity of symptoms, the individual patient feels wretched and often must refrain from customary play and school activities. The worry and perplexity of the parents further prevail on the physician for relief or cure within the shortest period of time. Some remission of symptoms is frequently noted a day or two after the onset of the illness, but a relapse just as commonly supervenes.

In a previous publication² it was pointed out that no convincing beneficial results with any therapeutic measures were obtained even for temporary relief in cases in which incapacity from the disease contributed to significant economic loss through absenteeism. I further stated that definitive therapy for this disease would depend on the isolation of a specific etiological agent. The discovery of the causal relationship between the Coxsackie viruses and pleurodynia now seems to have been established by a number of investigators.³

To combat and, if possible, to abort the painful and disabling symptoms of pleurodynia the use of the antibiotic aureomycin, which is effective in the treatment of several diseases of specific virus etiology, seemed indicated. Aureomycin was accordingly administered to 54 private patients ranging in age from 3 to 11 and over, in doses of 30 mg. per kilogram of body weight per day. There were 27 younger (3 to 6 years) and 27 older (7 to 11 or more) children. Thirty (56%) were boys, and 24 (44%) were girls.

The response of pleurodynia to aureomycin was rapid and often dramatic. Parents, instructed to report within 24 hours after administration of the drug was started, observed an obvious improvement after the second or third dose. In 40 of the 54 cases (74%), the rapid improvement involved almost complete disappearance of symptoms within the first 24 hours. In eight cases less dramatic but nevertheless favorable responses were obtained. In some of the cases in which the antibiotic seemed less effective the parents reported difficulty in administering the medication. In an occasional patient some slight residual tenderness was noted in the subcostal or epigastric regions of the abdomen subsequent to the disappearance of all other symptoms. Six patients were not benefited by aureomycin therapy.

In essence, aureomycin appeared to abort the clinical manifestations of pleurodynia. The relapse usually observed in an untreated patient was apparently prevented by administration of aureomycin in the successfully treated patients. The prevention of recurrent attacks is, for the present, not relevant to this consideration of therapy of acute, initial attacks of pleurodynia.

While the patient was receiving medication, physical activity was proscribed, and adequate rest for several days was advised. The earlier aureomycin was instituted after the onset of symptoms the more effective was the therapeutic response. In addition, it was my impression that the patients with an acute febrile type of the disease improved more quickly and completely with aureomycin therapy than those with a prolonged afebrile course. Most of the patients who did not respond to therapy had

the second type of pleurodynia, with a history of insidious, afebrile onset and a course of one week to two weeks' duration.

COMMENT

Dalldorf^{3c} has pointed out that although considerable data on the association of Coxsackie viruses with human disease have been published, scant attention has been paid to the clinical manifestations of infection by these agents. The recurrent nature of pleurodynia as described above provides additional information characterizing certain aspects of Coxsackie virus infections. The repeated clinical manifestations of this virus infection in the form of pleurodynia in the same person resembles other disease conditions with a virus etiology, like herpes simplex. The infected person appears to have an inherited susceptibility to repeated clinical attacks of the disease, which are precipitated by various excitant factors.

The ease with which many acute attacks of pleurodynia could be controlled with aureomycin seems to indicate the importance of further investigation of treatment of other Coxsackie virus infections with this or similar-acting antibiotics.

SUMMARY

There is need for further clinical clarification of many of the vague acute febrile illnesses associated with Coxsackie virus infections, of which many are unrecognized or subclinical. Epidemic pleurodynia represents a distinct clinical entity among these various syndromes, and, like them, occurs predominantly in children. The distinctive features of this disease in childhood are described and evaluated. A group of 17 patients with recurrent attacks of pleurodynia is reported. The significance of recurrence in relation to an altered concept of this epidemic disease is discussed. In a series of 54 cases of pleurodynia in children treated with aureomycin, 74% responded favorably.

672 Maccabees Bldg.

3. (a) Findlay, G. M., and Howard, E. M.: Coxsackie Viruses and Bornholm Disease, *Brit. M. J.* 1:1233 (May 27) 1950. (b) Hopkins, J. H. S.: Bornholm Disease, *ibid.* 1:1230 (May 27) 1950. (c) Dalldorf, G.: Coxsackie Viruses, *Bull. New York Acad. Med.* 26:329 (May) 1950.

The Father of Medicine.—In history, Hippocrates can well be called the Father of Medicine. He was a contemporary of Socrates, Aristotle and Plato. . . . He gave to Greek medicine its scientific spirit and its ethical ideas and was the first to recognize clinical inspection and observation. Instead of attributing disease to the gods or other fantastic imaginations he founded the bedside teaching method which has been the distinctive talent of all true clinicians. He possessed a high sense of dignity and lofty ideals of the medical profession and was a master in compiling accumulated knowledge of the preceding centuries. His permanent place in medicine is represented in the Hippocratic oath, for it is the earliest and still remains the most impressive document in medical ethics. . . . He has been called the master physician of all time, and his opinions became virtually law on medical subjects. Osler in one of his essays said that every physician ought to read some of Hippocrates every year to learn how to observe his patients. The greatness of Hippocrates is that he kept medicine on an equally high level with the work of the great lawmakers, philosophers, writers and artists of that era.—Donald C. Balfour, M.D., *The Lister Epoch in Medicine, Canadian Medical Association Journal*, November, 1951.

TREATMENT OF SUPERFICIAL DERMATOMYCOSES WITH ASTEROL® DIHYDROCHLORIDE

Harold G. Ravits, M.D., St. Paul

The antifungal activity of the benzothiazoles was first described in 1932.¹ Studies by Grunberg and his associates² have shown asterol® dihydrochloride (2-dimethylamino-6-[beta-diethylaminoethoxy]-benzothiazole dihydrochloride) to be of low toxicity and good solubility. In vitro studies by the same investigators have demonstrated its high fungistatic action, which is specific against various dermatophytes. Even at concentrations too low to prevent fungal growth, asterol® dihydrochloride modifies the morphological characteristics and metabolism of different types of fungi. In in vitro studies comparing growth-inhibiting concentrations, asterol® dihydrochloride was more effective against *Trichophyton gypseum*, *T. purpureum*, and *Microsporum audouinii* than an undecylenic acid-zinc undecylenate preparation. In a comparison of the two compounds in ointment form, asterol® dihydrochloride completely suppressed growth of *T. gypseum* and *M. lanosum*, whereas the undecylenic acid-zinc undecylenate preparation was much less effective against *T. gypseum*.

The purpose of this paper is to present an evaluation of the clinical use of asterol® dihydrochloride in the treatment of different types of superficial fungus infections of the skin. In the evaluation of this drug certain criteria were adhered to, as outlined by Herrick,³ with regard to selection of persons to be observed, diagnosis, control observations, observations during treatment, and number of subjects. The drug was used in three different forms: (a) as a 5% ointment in a polyethylene glycol (carbowax®) base, (b) as a 5% dusting powder, and (c) as a 5% tincture containing 70% alcohol. (Stritzler and his associates⁴ performed patch tests using different concentrations of asterol® dihydrochloride in ointment, tincture, and powder forms; they demonstrated that in 2 and 5% concentrations it is not a primary irritant or sensitizer, but that in a 10% concentration it is a primary irritant.) The 100 patients treated in this study came from the dermatological clinic of Ancker Hospital and from private practice. They were of all ages and both sexes, and their occupations and socioeconomic backgrounds were varied.

The clinical types of fungus infection treated were as follows: (a) tinea pedis, caused by *T. gypseum*, *T. purpureum*, and *Candida albicans*; (b) tinea cruris, caused by *Epidermophyton inguinale*, *C. albicans*, and *T. gypseum*; (c) tinea corporis, caused by *M. lanosum* and *E. inguinale*; (d) tinea capitis, caused by *M. audouinii* and *M. lanosum*; (e) tinea versicolor, caused by *Malassezia furfur*; (f) onychomycosis, caused by *T. gypseum*, *T. purpureum*, and *C. albicans*; (g) paronychia, caused by *C. albicans*; (h) pruritus ani, caused by *C. albicans*; and (i) thrush, caused by *C. albicans*. Cultures were taken from all patients prior to therapy. The scrapings were planted on a modified Sabouraud's agar and grown at room temperature. Positive cultures were not obtained in all cases. Downing and his co-workers⁵ have shown that pathogenic fungi are cultured in

approximately 37% of clinically mycotic infections. In the present study it was possible to identify the type of fungus present in 71% of the total (100) cases by elimination of those cases in which mycotic infection was clinically doubtful. All patients were treated on an out-patient basis and were instructed in proper application of the medication. It is conjectural whether treatment is carried out as instructed under such circumstances. All patients were observed at semiweekly or weekly intervals.

At the beginning of this study 20 patients were used as controls, and were treated with the ointment base, powder base, and tincture containing no asterol® dihydrochloride. All of these patients had tinea pedis, and only one showed improvement after two weeks of treatment with the nonmedicated base. The 19 patients who failed to respond to the inert bases after two weeks were subsequently given active medication. All were cured or showed noticeable improvement.

Tinea pedis.—Patients with tinea pedis comprised the largest group in the series. The clinical varieties ranged from mild scaling between the toes to acute erythematous vesicular eruptions. The predominating species of fungus encountered was *T. gypseum*. Of 54 patients treated in this group, 29 had been resistant to treatment with other fungicides, including the fatty acid preparations. Some patients used asterol® dihydrochloride powder in the morning and 5% asterol® dihydrochloride ointment at night. Others used the ointment twice daily and a few used the tincture and the ointment alternately. Ten patients in this group had an id eruption on the hands. They received the same treatment as the others, except that the id eruption was treated with a bland zinc lotion. Duration of treatment for the entire group ranged from one week to two months. In 24 patients (44.4%) the condition healed completely; in 24 it improved strikingly, and in 6 it failed to respond to treatment. Three of the six patients whose infection did not improve had an id eruption on the hands. The most dramatic results were obtained in patients with chronic cases of five to seven years' standing. They had been treated previously with many different fungicides, including the fatty acid preparations.

The asterol® dihydrochloride used in this study was supplied by Dr. M. J. Schiffrin of Hoffmann-LaRoche, Inc.

Read before the Section on Dermatology and Syphilology at the One-Hundredth Annual Session of the American Medical Association, Atlantic City, June 15, 1951.

From the Department of Dermatology and Syphilology, Ancker Hospital (Dr. John F. Madden, director), and the Division of Dermatology and Syphilology, University of Minnesota (Dr. H. E. Michelson, director).

1. Fungicides, Chem. Abst. 28: 4852, 1934.

2. Grunberg, E., and others: Mycological Studies with New Benzothiazole with Specific Activity Against Dermatophytes, Tr. New York Acad. Sc. 13: 22 (Nov.) 1950.

3. Herrick, A. D.: New Drugs, New York, Revere Publishing Co., 1946, p. 63.

4. Stritzler, C.; Fishman, I. M., and Laurens, S.: Treatment of Superficial Fungus Infections with New Antifungal Agent, Tr. New York Acad. Sc. 13: 31 (Nov.) 1950.

5. Downing, J. G.; Merrill, B., and Belding, D. L.: Clinical and Laboratory Study of Incidence of Fungi in Patients with Cutaneous Eruptions, New England J. Med. 222: 263 (Feb.) 1940.

Tinea cruris.—The group of patients with tinea cruris had infections of the upper thighs and intergluteal and inframammary areas. The organisms cultured were *C. albicans*, *E. inguinale*, and *T. gypseum*. Healing or improvement of the infection took from one week to three months. The ointment and powder were used on most of these patients. The tincture was found, in some instances, to be too irritating to the skin. Of the 18 patients treated, 10 (56%) showed complete healing, and 7 (39%) showed striking improvement. There was only one in whom the condition failed to improve.

Tinea capitis.—There were very few cases of tinea capitis available for treatment; therefore, this group can hardly be used as an indication of the effectiveness of asterol® dihydrochloride in such infections. The infections were caused by *M. lanosum* and *M. audouini*. For both types, treatment involved shaving of the infected scalp and twice daily (morning and evening) applica-

permits better penetration and, therefore, ultimate destruction of the fungus in the hair follicle and hair shaft. Reiss⁷ has shown that asterol® dihydrochloride has a high antisporulating index for hair infected with *M. audouini*.

Tinea versicolor.—Very satisfactory results were obtained in the treatment of tinea versicolor. The ointment was applied twice daily to the involved areas. One patient showed some irritation from the ointment and was then given the tincture form. All six patients had been infected for many years, and, in all, almost complete healing of the eruption occurred within the first week of treatment. Subsequent treatment resulted in healing the infection entirely. Determination of the ultimate result will depend on further observation, as this condition is known to be highly chronic.

Tinea corporis.—Four of the five cases of tinea corporis were caused by *M. lanosum*. The patients' response to therapy was fairly rapid and complete, as it is with any fungicide. The one case in which infection failed to heal completely was unusual in that the causative organism was *E. inguinale*. The patient's face, trunk, and extremities were involved, and the eruption had been present for five years. Previous treatment had included many antifungal agents, and desensitization with trichophytin vaccine. His response to asterol® dihydrochloride ointment was immediately good, but within a month's time he had a mild recrudescence of lesions on the face and buttocks.

Paronychia.—Four patients with paronychia caused by *C. albicans* were treated with applications of the tincture, followed by applications of the ointment. These infections healed completely. Duration of treatment ranged from 4 to 10 weeks. These patients were cautioned to avoid immersion of the infected fingers in water or any solution.

Onychomycosis.—Of three cases of onychomycosis, one was caused by *T. gypseum*, one by *T. purpureum*, and the third by *C. albicans*. Treatment involved application of asterol® dihydrochloride tincture daily and the ointment twice daily. All three patients had fingernail and toenail involvement of several years' duration. Previous treatment had included many of the well-known fungicides, including ammoniacal silver nitrate and the fatty acid preparations. In the patient with *T. purpureum* infection there was no improvement after three months' treatment. In the other two considerable improvement was evident after four months' treatment. Meticulous care and cooperation by these patients was most important in their treatment. Careful filing of the involved nails to almost paper thinness was essential. The tincture in one case was found to be too drying and appeared to accentuate the brittleness of the nails.

Pruritus ani.—Three patients with pruritus ani, from which *C. albicans* was cultured, were treated with the ointment. The perianal dermatitis healed with treatment, but the pruritus persisted. This is consistent with the psychogenic etiology of pruritus ani and the saprophytic nature of *C. albicans* under certain circumstances.

Thrush.—In one infant an extensive *C. albicans* infection in the mucous membranes of the mouth healed

Results of Treatment of Superficial Dermatomycoses with Asterol® Dihydrochloride

Type of Infection	No. of Cases	Organism Cultured	Cured	Noticeably Improved	Unimproved
Tinea pedis.....	17	T. gypseum	10	7	0
	5	T. purpureum	2	3	0
	8	C. albicans	3	4	1
	24	No growth	9	10	5
Tinea cruris.....	10	C. albicans	5	5	0
	2	E. inguinale	2	0	0
	1	T. gypseum	1	0	0
	5	No growth	2	2	1
Tinea capitis.....	2	M. lanosum	2	0	0
	4	M. audouini	3	0	1*
Tinea versicolor.....	6	M. furfur	6	0	0
Tinea corporis.....	4	M. lanosum	4	0	0
	1	E. inguinale	0	1	0
Paronychia.....	4	C. albicans	4	0	0
Onychomycosis.....	1	T. gypseum	0	1	0
	1	T. purpureum	0	0	1
	1	C. albicans	0	1	0
Pruritus ani.....	3	C. albicans	0	0	3
Thrush.....	1	C. albicans	1	0	0
Total.....	100		54	34	12

* Still undergoing treatment.

tion of the tincture and ointment preparations of asterol® dihydrochloride. The liquid was applied and allowed to dry; then the ointment was applied. The patients' scalps were checked by Wood's light examination at weekly intervals, at which time all fluorescent hairs were manually epilated. Three patients with *M. audouini* infection were cured after one, two, and three months' treatment respectively, and two patients with *M. lanosum* infection were cured after six weeks' treatment. The one patient whose condition has not improved has been undergoing treatment for five months. The long, tedious treatment of tinea capitis indicates the need for an antifungal preparation that will cure this type of fungus infection rapidly. Asterol® dihydrochloride appeared to be superior to other preparations in the treatment of tinea capitis; however, it is emphasized again that a definitive judgment can not be made on the basis of so few cases. It has been reported⁶ that the keratolytic action of this preparation

6. Schnitzer, R. J.: Personal communication to the author.
7. Reiss, F.: Antisporulating Effect of Asterol Dihydrochloride, Tr. New York Acad. Sc. 13: 28 (Nov.) 1950.

after two days' treatment with asterol® dihydrochloride tincture. The medication was applied locally to the lesions with a cotton applicator.

SUMMARY

Asterol® dihydrochloride was used in the treatment of various clinical types of superficial fungus infections of the skin. Of 100 patients treated, infection was completely cured in 54, considerably improved in 34, and showed no improvement in 12. Many of the patients whose infections were either cured or improved had had infections of long standing and had previously been

treated with many different fungicides, including the fatty acid preparations, dyes, ammoniacal silver nitrate, permanganate soaks, and benzoic and salicylic acid (Whitfield's) ointment. Gratifying results were obtained in tinea pedis, tinea versicolor, tinea capitis, tinea corporis, and paronychia. Unsatisfactory results were noted in pruritus ani and onychomycosis. No adverse reactions, either systemic or local, resulting from application of asterol® dihydrochloride were observed in this group of patients.

350 St. Peter St.

RESULTS OF SURGICAL TREATMENT OF UNILATERAL CARCINOMA OF BREAST IN WOMEN

Stuart W. Harrington, M.D., Rochester, Minn.

Malignant disease of the mammary gland is important in the general cancer program because the mammary gland is the commonest site for malignant disease in women. From the standpoint of treatment, probably no other type of malignant disease has been treated surgically in more instances, over a longer period of time, or with better results, but still no method of operative treatment is generally accepted by the medical profession. However, it is generally accepted that, up to the present, the only therapeutic agents, utilized singly or in combination, that have been valuable in treatment of carcinoma of the mammary gland are surgical procedures, radium, roentgen rays, and hormones. I believe that the most effective treatment for carcinoma of the mammary gland is radical surgical treatment and that the results can be improved by instituting this treatment earlier in the course of the disease. Roentgen therapy following radical surgical treatment in some instances improves the results of operative treatment in certain types of lesions.

The outstanding features of statistical studies of carcinoma of the breast are the alarming increase in frequency as well as the increase in mortality from the disease. In the United States the mortality rate of carcinoma of the breast per 100,000 women was 10.9 in 1901, and had increased to 26.9 in 1948. During that year (1948) 18,938 women died of carcinoma of the breast, which is the greatest annual number of deaths resulting from the disease ever recorded.

The significance of these statistics, as well as the fact that many patients delay seeking medical advice in regard to conditions of the breast, has led to an intensive educational program in which patients are warned not to disregard any breast abnormalities. Members of the medical profession have participated in this program for many years. The program has increased the physician's responsibility to the patient, since the objective is to persuade the patient to submit to examination early before the classic signs of malignant disease are evident. The obligation of the physician who makes the first examination is to establish a definite diagnosis or to make certain that a definite diagnosis is established for all patients he observes.

SIGNS AND SYMPTOMS

There are no pathognomonic signs or symptoms by which all malignant growths can be recognized clinically. Unfortunately this is particularly true of early lesions and indicates the importance of considering every lesion of the breast potentially malignant. The clinical manifestations depend on the duration of the malignant lesion at the time of examination; signs and symptoms of early malignant disease are hopelessly inadequate as a basis for diagnosis. If sufficient time is permitted to elapse, it is probable that 100% of these lesions can be diagnosed clinically, but meanwhile much valuable time has been lost before treatment is instituted, and in most instances the patient will have lost any chance of obtaining permanent cure with surgical treatment.

RADICAL SURGICAL TREATMENT

The results of treatment of malignant disease of the breast were greatly improved by radical surgical treatment. Since the introduction of radical mastectomy by Halsted, it has been the method of treatment most generally accepted by the medical profession. The rationale for radical surgical treatment is that the malignant lesion is localized at the onset and later in the course of the disease invades other tissues by transmission through the lymph stream and occasionally through the blood stream. If this conception of the disease is correct, the most important considerations in treatment are early recognition and immediate complete removal of the diseased tissues. If the condition is confined to the breast at the time of operation, complete eradication of the disease can be expected. One of the principal reasons for failure of surgical operation to accomplish this objective in every case is the high percentage of cases in which metastasis occurs before operation is performed.

From a surgical standpoint, malignant lesions of the breast may be divided into two general groups. The first group consists of those that can be diagnosed clinically as malignant. These lesions are best treated by immedi-

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ate primary radical mastectomy. The second group consists of the lesions that cannot be diagnosed from the clinical manifestations of the disease. This is the most important group from a surgical standpoint, since they are usually early lesions and can be treated most satisfactorily by surgical means. A single localized indurated region or tumor should be removed completely by wide surgical excision and a definite diagnosis should be established immediately by microscopic examination of frozen sections. If the lesion is found to be malignant, the operation should be completed immediately as a radical mastectomy.

The best results in treatment of carcinoma of the breast are obtained with primary radical mastectomy. Methods of performing the minor technical details vary greatly, but the fundamental principles are invariable and should be followed in every such operation. As initial treatment this is by far the most important procedure, and the possibility of a cure depends on the thoroughness with which it is carried out. The importance of radical mastectomy cannot be overestimated, for secondary operative procedures are rarely curative. I believe that one of the important factors in the unsatisfactory results obtained from surgical treatment is the

findings. I have accepted for operation all patients to whom I felt there was a reasonable chance of offering comfort or longer life, as well as those for whom I felt there was a reasonable chance of cure. It may seem that these rules of operability have not been drawn strictly enough and that patients who had too extensive growths have been accepted for operation. This is a matter of opinion, however, and justification has been found in many cases in which the condition was thought to be hopeless before operation but the patients lived to enjoy years of comfort.

Factors That Influence Results.—The more important factors that influence the results of radical surgical treatment are the extent of the malignant involvement at the time of operation; the thoroughness with which the radical operation is performed; the degree of malignancy as shown by microscopic examination of the primary lesion; the presence of other associated conditions, such as pregnancy and lactation; the presence of general constitutional diseases, such as diabetes; and the age of the patient.

I recently made a study of all the cases of unilateral carcinoma of the breast in women treated surgically by radical mastectomy at the Mayo Clinic in the 37 years

TABLE 1.—Influence of Axillary Metastasis on Survival Rate Following Radical Mastectomy

Axillary Metastasis	Totals in Study	No. of Years of Survival After Operation														
		3 or More			5 or More			10 or More			15 or More			20 or More		
		No. Traced	No.	% *	No. Traced	No.	% *	No. Traced	No.	% *	No. Traced	No.	% *	No. Traced	No.	% *
Present.....	4,664	4,593	2,138	46.5	4,331	1,406	32.5	3,579	644	18.0	2,918	351	12.0	2,302	172	7.5
Absent.....	3,410	3,357	2,903	86.5	2,994	2,344	78.3	2,231	1,365	61.2	1,645	793	48.2	1,242	452	36.4
Total.....	8,074	7,950	5,041	63.4	7,325	3,750	51.2	5,810	2,009	34.6	4,563	1,144	25.1	3,544	624	17.6

* Based on patients traced by inquiry as of Jan. 1, 1950. Included in the three-year group are only those patients who were operated on three or more years prior to the time of inquiry, that is, 1946 or earlier; the five-year group includes only those patients operated on in 1944 or earlier, and so forth.

relative frequency with which minor operations are performed for malignant disease.

Operability.—Inasmuch as the extent of the disease is such an important factor in the success of operative treatment, it is obvious that the results depend on the type of lesion treated by this means. Opinions vary as to what determines operability. In the series of cases from the Mayo Clinic that are reported here, any lesion of the breast was considered operable if it was freely movable from the thoracic wall, regardless of ulceration. In some cases, even if there were cutaneous nodules proximal to the tumor and regardless of the presence or absence of palpable axillary lymph nodes, the lesion was considered operable. In addition, patients were accepted for operation if they had a diffuse type of malignant growth and if malignant disease was associated with lactation or pregnancy. Lesions were considered to be inoperable when a large growth was attached to the thoracic wall and there was extensive metastasis to the axillary and supraclavicular lymph nodes or to other distant parts of the body. A few patients who had metastasis involving distant portions of the body were accepted for operation because of exceptional circumstances.

Thus it is difficult to make any sharp distinction between operable and inoperable lesions and in each case treatment must be determined according to the

from 1910 through 1946. Three-year survival rates following operation were compiled in a series of 8,074 cases.

METHODS OF STUDY

The study of survival rates for the various periods after operation was made in the following manner. All women treated by radical mastectomy, regardless of the type or extent of their disease or other associated conditions, were included in this study. The records of patients who had undergone operation the requisite number of years prior to the time of inquiry (Jan. 1, 1950) were selected first. For the calculation of the 3-year survival rate, the patients who had an operation in 1946 or earlier were selected; for the 5-year survival rate, those who had an operation in 1944 or earlier were selected; for the 10-year survival rate, those who had an operation in 1940 or earlier were selected, and so forth. Obviously, then, the 3-year survival rate was calculated on a larger number of patients than the 5-year survival rate; the 5-year rate on a larger number of patients than the 10-year survival rate, and so forth. Any patient not traced for a sufficient number of years after operation was considered untraced, and was not included in the calculation of the survival rate. For instance, in calculating the five-year survival rate, a patient who had undergone operation seven years prior to the time of inquiry but had been traced for only four years after operation and who was living at that time, was considered untraced in the calculation of the five-year survival rate because it is not known whether she survived until the fifth year after operation. In calculation of the three-year survival rate, the patient was considered traced, for it is known that she survived more than three years after operation.

When patients did not answer the routine follow-up letter, the local department of health, bureau of vital statistics, or other

agency was consulted to learn whether any record of death existed. Of the patients on whom operation had been performed three or more years before investigation, 98.4% were traced for the requisite period. In all of these statistical studies of survival rates it has been assumed that the patient died of malignant disease, although in many instances it was definitely known that death was due to other causes.

PRESENCE OR ABSENCE OF METASTASIS TO AXILLARY NODES

The most important factor in the prognosis following surgical treatment is the extent of the disease at the time of operation. I do not believe that clinical classifications of the extent of the disease are uniform or accurate enough for comparison of the results from surgical treatment of the various types of lesions encountered. In my opinion the most important consideration is whether or not the disease has metastasized from the primary location in the breast before operation. This is most accurately determined by definitely proving the presence or absence of axillary nodal metastasis at the time of operation. A comparison of cases with nodal metastasis and those without nodal metastasis shows that the prognosis is much more favorable in cases in which there is no axillary involvement (table 1). The three-year survival rate was calculated for 8,074 patients with unilateral carcinoma of the breast on whom operation was performed in 1946 or earlier, of whom 7,950 (98.4%) were traced. The survival results varied widely, and the prognosis was much better in those cases in which axillary nodal metastasis was not found at the time of operation than in those cases in which axillary nodal metastasis was found.

Although axillary nodal metastasis is only one indication of the extent of the disease at the time of operation, I believe that it is one of the most important factors affecting the prognosis. Therefore, in compilation of survival rates of malignant disease of the breast, I believe that all cases should be considered in two groups, those with and those without axillary nodal metastasis at the time of operation, and that statistical studies should never be based on a combination of the groups without indicating the number of patients in each group.

RESULTS IN FIVE-YEAR PERIODS FROM 1910 THROUGH 1944

A quinquennial study was made of unilateral carcinoma of the breast in women who had had radical mastectomy in the years 1910-1944 to determine whether there had been any improvement in the results of surgical treatment during these different periods. This study was based on 7,445 patients, of whom 7,325 were traced. The patients are divided into two groups, those with and those without axillary nodal metastasis at the time of operation (table 2). A consistent and appreciable improvement in the results obtained from radical mastectomy in each succeeding five-year period is evident. The study shows that 23.4% of patients who had axillary nodal metastasis at the time of operation in the years 1910-1914 were living five years after operation, as compared with 39.4% of those on whom operation was performed during the five-year period 1940-1944. Better results were obtained among patients without nodal metastasis in the same period. Among those who

underwent operation in the five years 1910-1914, 62.6% survived five years, as compared with 85.6% in the period 1940-1944.

GRADE OF MALIGNANCY

A study was made to determine whether there was any difference in the results obtained in treatment of different grades of carcinoma of the breast. The cases have been graded according to Broders' method of dividing malignant lesions into four grades based on cellular differentiation. This part of the study is based on 7,012 cases, the total number in which lesions have been graded in this series. A study also was made to determine the percentage of cases in which each of the four grades of malignancy was present and the percentage of cases of each grade of malignancy with and without axillary nodal metastasis at the time of operation (table 3). In 47.5%, or nearly half, of all cases of carci-

TABLE 2.—Five-Year Survival Rates After Radical Mastectomy During Different Five-Year Periods

Period of Operation	With Metastasis			Without Metastasis			Totals		
	No. Traced	No.	%*	No. Traced	No.	%*	No. Traced	No.	%*
1910-1914	303	71	23.4	214	134	62.6	517	205	39.7
1915-1919	592	155	26.2	294	210	71.4	886	365	41.2
1920-1924	659	156	23.7	360	252	70.0	1,019	408	40.0
1925-1929	762	248	32.5	399	308	77.2	1,161	556	47.9
1930-1934	612	216	35.3	403	329	81.6	1,015	545	53.7
1935-1939	662	268	40.5	589	482	81.8	1,251	750	60.0
1940-1944	741	292	39.4	735	629	85.6	1,476	921	62.4
Total	4,331	1,106	25.5	2,994	2,344	78.3	7,325	3,750	51.2

* Calculated as in table 1.

TABLE 3.—Metastasis Correlated with Grade of Malignancy of Unilateral Carcinoma of the Breast at Time of Radical Mastectomy

Grade	Totals		With Metastasis		Without Metastasis	
	No.	%	No.	%	No.	%
1	538	7.7	12	2.2	526	97.8
2	809	12.4	285	32.8	524	67.2
3	2,271	32.4	1,397	61.1	874	38.9
4	3,334	47.5	2,676	80.3	658	19.7
Total	7,012	100.0	4,360	62.2	2,652	37.8

noma of the breast in this series the degree of malignancy was graded 4, and axillary nodal metastasis was present in 80.3% of all cases of grade 4 lesions at the time of operation. When the data concerning grade 3 and 4 lesions were totaled, it was found that in 79.9% of cases of carcinoma of the breast there was a high degree of malignancy from which metastasis occurs early. These data emphasize the seriousness of malignant disease of the breast in that the majority of the lesions are of a high grade of malignancy and have metastasized to axillary nodes at the time of operation.

A study was then made to determine the survival rates of patients with and without axillary nodal metastasis according to grade of malignancy (table 4). The results show a definite and uniform relationship between the operative results and the grade of malignancy; the lower the grade of malignancy the higher the percentage of patients alive 3, 5, and 10 years after operation. This was found to be true both when axillary metastasis was present and when it was not. This study also corrob-

orates the findings in the previous study that the surgical results in cases in which the grade of malignancy is the same are much more satisfactory in cases without metastasis to the axillary nodes than in those with metastasis. The study shows that the grading of malignant lesions gives an important indication as to the prognosis. I believe that the grading of malignant lesions represents one of the greatest advances that has been made in the study of malignant disease in recent years.

IRRADIATION

Five-year survival rates following radical mastectomy were studied for successive five-year periods to determine the results obtained for those patients with and

metastasis were given irradiation therapy as compared with 530 patients who did not receive irradiation therapy. This difference in number is even more apparent in the different five-year periods and makes an inequitable comparison for study, particularly on a percentage basis, since one case would make a much greater difference in the percentage in the smaller group of cases.

Another factor to be noted in this study is that irradiation therapy was considered routine postoperative treatment for all patients who had axillary nodal metastasis from 1920 through 1944. Patients did not receive irradiation only because of some complicating general condition that contraindicated its use. These conditions make the prognosis in this group less satisfactory. In

TABLE 4.—Unilateral Carcinoma of the Breast With and Without Axillary Metastasis at Time of Radical Mastectomy: Comparison of Survival Rates According to Grade of Malignancy

	No. of Years of Survival After Operation														
	3 or More			5 or More			10 or More			15 or More			20 or More		
	No. Traced	No.	% *	No. Traced	No.	% *	No. Traced	No.	% *	No. Traced	No.	% *	No. Traced	No.	% *
With Metastasis															
Grade 1.....	12	11	91.7	12	11	91.7	11	7	63.6	11	5	45.5	11	4	36.4
Grade 2.....	279	200	71.7	261	149	57.1	219	81	37.0	192	50	26.0	168	23	13.7
Grade 3.....	1,361	789	58.0	1,288	512	39.8	1,019	205	20.1	816	100	12.3	673	44	6.5
Grade 4.....	2,613	1,008	38.1	2,473	612	26.0	2,034	293	14.4	1,604	153	9.5	1,161	74	6.4
Without Metastasis															
Grade 1.....	519	502	96.7	423	401	91.8	239	211	88.3	134	106	79.1	76	49	64.5
Grade 2.....	577	532	92.2	526	454	86.3	389	267	68.6	268	135	50.4	160	57	35.6
Grade 3.....	867	732	84.4	763	556	72.9	520	292	56.2	331	146	44.1	193	58	30.1
Grade 4.....	648	513	79.2	551	381	69.1	355	168	47.3	210	75	35.7	149	38	25.5

* Calculated as in table 1.

TABLE 5.—Five-Year Survival Rates After Radical Mastectomy With and Without Postoperative Irradiation for Different Five-Year Periods

Period of Operation	With Metastasis						Without Metastasis					
	With Irradiation			Without Irradiation			With Irradiation			Without Irradiation		
	No. Traced	No.	% *	No. Traced	No.	% *	No. Traced	No.	% *	No. Traced	No.	% *
1915-1919.....	361	101	28.0	231	54	23.4	163	117	71.8	131	93	71.0
1920-1924.....	599	141	23.5	60	15	25.0	263	182	69.2	97	70	72.2
1925-1929.....	668	223	33.4	94	25	26.6	249	195	78.3	150	113	75.3
1930-1934.....	562	202	35.9	50	14	28.0	286	235	82.2	117	94	80.3
1935-1939.....	616	255	41.4	46	13	28.3	416	340	81.3	171	142	83.0
1940-1944.....	692	274	39.6	49	18	36.7	177	137	77.4	558	492	88.2
Total.....	3,498	1,196	34.2	530	139	26.2	1,556	1,206	77.5	1,224	1,004	82.0

* Calculated as in table 1.

without axillary nodal metastasis who had irradiation subsequent to operation as compared with those who did not have irradiation subsequent to the operation (table 5). This study was made for the 30 years 1915-1944, since irradiation therapy was instituted as postoperative treatment in 1915. The results in the different five-year groups were not uniform or consistent. In the five years, 1920-1924, the results were more satisfactory in patients who did not receive postoperative irradiation than in those who did. In the other periods, the results were more satisfactory in patients who had postoperative irradiation than in those who did not have it, and there was an over-all improvement of approximately 8% in patients who had irradiation as compared with those who did not have it.

It should be remembered, however, that there is considerable difference in the total number of patients treated in each group; 3,498 patients with axillary nodal

most of these cases roentgen treatment was attempted and had to be discontinued.

In the cases without axillary nodal metastasis, a greater percentage (82.0%) of patients who did not have irradiation therapy than of patients (77.5%) who did have postoperative irradiation therapy were living five years after operation. In this study there is a more equitable number for comparison in that the total number not treated by irradiation therapy was 1,224 as compared with 1,556 who received postoperative irradiation therapy.

The results obtained in this study are not uniform or consistent. In three of the five-year periods results were more favorable in from 1 to 3% of patients who had irradiation therapy and in three of the five-year periods the five-year results were more favorable in from 2 to 11% of patients who did not have postoperative irradiation therapy.

The study shows that the results obtained from radical mastectomy in patients who did not have axillary nodal metastasis at the time of operation were not improved by irradiation therapy. In fact, 4.5% more of these patients who did not receive irradiation therapy than of those who did lived for five years or more after operation.

TABLE 6.—Factors Influencing Prognosis of Radical Mastectomy for Carcinoma of Breast in 7,822 Patients*

Diagnosis or Associated Factor	%	With Axillary Metastasis Who Lived More Than					
		3 Yr.	5 Yr.	10 Yr.	15 Yr.	20 Yr.	
Unilateral carcinoma.....	58.8	46.3	32.8	19.4	11.0	9.2	
Paget's disease.....	44.3	44.7	26.5	14.3	5.6	0	
Pregnancy or lactation.....	75.7	18.7	8.9	5.1	2.5	1.5	
Subsequent pregnancy.....	36.4	82.1	61.1	51.4	38.5	27.8	
Associated diabetes.....	67.7	43.9	30.6	9.5	0	0	
Previous bilateral oophorectomy	51.0	14.4	20.0	14.6	12.1	9.1	
Bilateral carcinoma, simultaneous	62.3	33.3	27.7	5.4	0	0	
Bilateral carcinoma, non-simultaneous	18.9	61.7	42.3	23.7	16.2	16.7	

		Without Axillary Metastasis					
		3 Yr.	5 Yr.	10 Yr.	15 Yr.	20 Yr.	
Unilateral carcinoma.....	41.2	86.8	78.6	63.6	52.9	43.0	
Paget's disease.....	55.7	88.2	85.7	67.9	42.1	35.7	
Pregnancy or lactation.....	24.3	72.7	64.5	54.2	41.2	33.3	
Subsequent pregnancy.....	63.6	100.0	98.5	92.3	79.5	69.0	
Associated diabetes.....	32.3	71.2	60.7	32.9	41.4	16.7	
Previous bilateral oophorectomy	46.0	78.3	69.8	52.9	42.3	28.0	
Bilateral carcinoma, simultaneous	37.7	69.0	57.7	44.4	25.0	20.0	
Bilateral carcinoma, non-simultaneous	51.1	83.9	78.5	59.1	42.2	26.5	

* Survivals calculated as in table 1.

A true evaluation of irradiation therapy can be obtained only by comparing similar types of cases in which operation was performed. These studies of five-year survival rates indicate that (1) in cases of mammary carcinoma with axillary nodal metastasis, there has been some improvement in the results when radical mastectomy was followed by irradiation therapy; and (2) in cases without axillary nodal metastasis the results of

radical mastectomy with or without irradiation therapy were usually essentially the same; but, in a certain percentage of cases, the results of radical mastectomy with irradiation were less satisfactory. At present, irradiation therapy is given at the Mayo Clinic in all cases in which nodal metastasis is present at the time of operation unless it is contraindicated by some general condition, but irradiation therapy is not being used in cases in which no axillary nodal metastasis is found at the time of operation. These studies indicate that the effectiveness of irradiation depends on the type as well as the extent of the disease, and the most important consideration in the treatment of adenocarcinoma of the breast is thorough primary radical mastectomy.

OTHER FACTORS INFLUENCING PROGNOSIS

Limited space does not permit me to present the complete detailed study that has been made of various other factors that influence prognosis and results of radical surgical treatment. All of these different groups except the cases of bilateral carcinoma of the breast are included in the general statistical study. I am including a summary of the survival rates of these different groups, including patients with Paget's disease, patients with carcinoma during pregnancy or lactation, patients who had subsequent pregnancies, those who had associated diabetes, or bilateral oophorectomy for nonmalignant disease at least one year prior to radical mastectomy for carcinoma of the breast, patients with carcinoma simultaneously in both breasts, and those who had carcinoma in the remaining breast subsequent to radical mastectomy of one breast (table 6).

These results, compared with the results obtained in the entire group of cases of unilateral carcinoma are better in cases without axillary nodal metastasis than in those with axillary nodal metastasis, and confirm the importance of instituting surgical treatment early in the course of the disease before metastasis has occurred.

MODERN ADVANCES AND TRENDS IN MILITARY MEDICINE

Rear Admiral Lamont Pugh (MC), U. S. N.

Military medicine during the centuries from Homer's Trojan War to the present Korean conflict has steadily advanced toward a higher state of excellence. The trend over the years has been toward increasing military recognition for the medical services and improving professional competence for medical personnel. Today the military physician in all respects is in the front rank. He has become so professionally astute and so versed in the strategy and tactics of battle that his medical counsel is highly respected and his participation in matters of logistics is routinely sought.

When we view the military physician today carefully and scientifically planning his operations, we realize how long a road he has traveled from the days of the Napoleonic Wars, when a Scot, Sir Gilbert Blane, prompted by his recognition and appreciation of the monumental work of James Lind, another Scot (whose name incidentally is held by historians to be the greatest in naval medicine), secured adoption by the British Royal Navy

of regulations requiring the use of lemon juice aboard ship to prevent scurvy and the use of vaccine to prevent smallpox. These two reforms of themselves started the military physician on his upward path to recognition.

By the middle of the 19th century medical officers had been granted military rank compatible with their military and professional qualifications, and had been given due authority over medical care and medical supply. The concept that medical care and medical supply—that the doctor and his bag in the military as well as elsewhere—comprise two parts of one and the same entity has, for over a century in this nation, through four wars and part of a fifth fracas that at least smacks of war, been accepted as axiomatic. The validity of this philosophy, however, has recently been seriously challenged in the Navy and, as a consequence, management

Surgeon General of the United States Navy
Read before the Fifth Annual Clinical Session of the American Medical Association, Los Angeles, Dec. 7, 1951.

control of the Navy's medical supply system is being transferred to the Bureau of Supplies and Accounts.

There has never been anything static about medicine, and this is particularly true of military medicine. War has always been a stimulus to medical and surgical advancement. Much of the work that is now going on to find a suitable substitute for blood plasma, a search that has resulted in such products as dextran, polyvinylpyrrolidone ("periston"), "oxypolygelatin," and other gelatins, has received its major stimulus from the military. The creation of new military medical problems stimulates new medical discoveries and these discoveries, in turn, contribute greatly to scientific progress and mechanical developments. This must be particularly apparent in such fields as submarine and aviation medicine. The atomic bomb also created a new complex of military medical problems in 1945, and today we face a situation of very rapid change in all aspects of military affairs, including medicine. To some degree we have to plunge into the unknown and prepare for military contingencies that have never occurred before.

After 1945, as after most wars, there was a slackening of popular interest in military power, military preparedness, and military medicine. For an extended period emphasis at the highest policy level appeared to be placed on economy. Numerous studies were made by committees or boards that issued reports and offered proposals for the reorganization and reduction of our military forces. We had to justify and explain our expenditures many times. But from that experience we learned much, and now some semblance of order begins to appear.

DOCTRINE OF UNIFICATION

When our vision imagines distant goals, the detailed outlines of the vision are not plain, and only trial and error produce the whole edifice we intend to create. But certain creations by this time have sufficiently clear forms to be recognized as new entities. These have stemmed in a large measure from the doctrine of unification, a doctrine that everyone favors but hardly anyone can define precisely. At the same time they are the product of evolution rather than revolution. While it is difficult to say what the ultimate result will be with respect to this philosophy of unification, it is nevertheless possible to visualize a reasonably stable pattern, evidenced by the following accomplishments:

1. Joint and common instruction is being conducted in appropriate special fields, such as the medical aspects of atomic energy, biological and chemical warfare, and aviation medicine.

2. We have integrated our hospital services so that the patients from any one service may be hospitalized in the hospitals of any other service. Whether the hospital is the nearest and the best staffed and equipped to care for the patient is the primary consideration.

3. Concomitant with joint hospitalization we have joint staffing of facilities that have patients from two or more services. Thus there is a considerable interchange of physicians, both those with general capabilities and those qualified as specialists. Joint staffing promotes economy in the number of hospitals the armed forces must maintain by promoting consolidation; it also makes

possible the most effective utilization of scarce personnel.

4. We now have joint Army and Navy purchasing of medical and dental supplies and equipment, through the Army-Navy Medical Procurement Agency. A single standard medical supply catalog is in daily use.

5. The Army's Institute of Pathology has become the Armed Forces Institute of Pathology, with a rotating directorship.

6. The Surgeon General's Library, maintained by the Army since 1836, will in the future be the Armed Forces Medical Library, and will have rotating directors chosen from the three services.

7. An *Armed Forces Medical Journal* has supplanted the Navy's *Naval Medical Bulletin* and the *Bulletin of the U. S. Army Medical Department*. This joint publication not only saves money and personnel but also enables the editor, who represents the three services by rotation, to draw on a richer and more informative selection of manuscripts.

8. Interservice unity has been achieved with respect to sea transportation. At one time the Army operated its own fleet of transports and auxiliary vessels; in fact it once operated more vessels on the waters of the world than did the Navy. Now all the crafts that float on the surface of the sea, except a few vessels that belong to the Army Engineers who are responsible for rivers and harbors, belong to the Navy. The Military Sea Transportation Service has been created under the directorship of the Navy, and it includes all military sea transports.

9. An *Armed Services Medical Regulating Office* has been set up in Washington to place patients returning from overseas in the service hospital nearest their homes or in the hospital that will most nearly satisfy the desires of the individual. The movement of the average patient from the front line aid station to the port of debarkation in the United States and subsequently to a hospital for definitive treatment is now arranged according to a carefully devised plan based on the many lessons in evacuation learned in former wars.

10. The supply by one service of the medical material needs of all three services is being given a trial.

The agency that coordinates this joint activity is the *Armed Forces Medical Policy Council*. This consists of a civilian chairman and three civilian members, one of whom is a dentist, and the three surgeon generals of the medical departments of their respective services. The council has contacts with other military offices such as the Joint Chiefs of Staff, with federal agencies such as the National Research Council and Selective Service System, and with private medical and dental associations. The council serves especially as a group to carry out joint studies, to coordinate joint training, and to perform necessary liaison work in connection with such general programs as procurement of whole blood and production of plasma. Each medical department retains control of the medical logistics operations entailed in support of its own combatant forces.

Another advance worthy of mention is the creation in the American Medical Association of a separate Section

on Military Medicine. You are aware that almost 100 years ago (1859) the Association was first organized into sections for the purpose of performing such parts of its scientific labor as might relate to particular branches of medicine and surgery. The new Military Medicine Section should become an excellent forum in which information and views can profitably be exchanged on this special phase of medical practice. Both military and civilian physicians in meetings of the Association will have the convenient opportunity to listen to papers and discussions pertaining to both military and civilian medicine.

While unity and integration of the three medical services have been to a large degree achieved, each service retains a high degree of individuality. Each medical service seeks to maintain an organization best adapted to the support of its own operating forces. This mission can be fulfilled best if each service has its own medical department, responsible and accountable directly and independently to its own service.

It has been said that medicine, like any other science, will remain alive and progressive to a degree commensurate with the degree in which it engages in research. The medical departments of the armed services steadfastly insist, and quite rightly so, on directing their individual research programs. Denied the opportunity and right to conduct its own research program, it is believed that the quality of any of the medical departments would soon decline, that the interest of its medical officers would stagnate and fade, and that its stature as a medical organization would retrogress to that of a minor constituent. Some of this research is done separately when it concerns a matter of interest only to a single service as, for instance, research in problems related to submarine operations that would be of concern only to the Navy. Research projects in which the crux is of concern to all three services are participated in jointly. The effect of exposure to extreme cold would be a fair illustration, and there are moreover certain projects in which the military and civilian interests are similarly at stake. An illustration of a research project in which the military and civilian experts are jointly engaged is the research in effort to find a satisfactory substitute for blood plasma. All of the research being pursued within or by the medical departments of the armed services is closely screened by several agencies, including the research and development board of the individual service and of the Department of Defense and, when desired, by the National Research Council. Through the years military medicine will, I am sure, work closely with civilian medicine to better methods of protecting and strengthening the minds and bodies of our fellow beings. Today we stand side by side facing the changes of tomorrow with the faith and determination that through our hands a strong, healthy world shall evolve.

MEDICAL ADVANCES IN KOREA

Along with the aforementioned examples of cooperation among the three services, I should like to point out some of the more notable developments and advances of a medical nature that have been made as a result of the Korean conflict. The use of helicopters in Korea to evacuate casualties for short distances and of transport planes to convey them over long distances cer-

tainly constitutes a most notable advance. In many cases, as when wounded men have been cut off from the remainder of the division, use of the helicopter, when we have control of the air, is the only way field casualties can be brought out safely and given early definitive care. It is especially useful in evacuation from difficult terrain such as that in Korea, where the automotive ambulance often faces insuperable obstacles. The helicopter is ideally suited for transporting casualties with severe abdominal or chest wounds who cannot withstand the rigors of a long jolting ambulance ride.

To facilitate evacuation to hospital ships by helicopter, landing platforms are being installed aboard our hospital ships, which will enable wounded patients to be set down easily and quickly aboard these floating hospitals. The *U. S. S. Consolation* has been so equipped, and we intend to equip all our hospital ships with helicopter landing platforms as they go to the Navy yard for overhaul. It has moreover been the recommendation of the division surgeon with the First Marine Division in Korea that helicopters be made a part of the basic equipment provided medical battalions serving with forces in the field. Thus, the mobility of medical support of amphibious and field medical operations may be greatly augmented.

Transport planes are used to convey patients over longer distances. Air trips have great advantages in speed, flexibility, and frequency. Moreover, the ability to move patients rapidly, comfortably, and safely from all points of the world to highly qualified specialists concentrated in relatively few medical centers makes the services of these specialists available to the greatest number of personnel. The percentage of patients returned to the United States by air increased from 30% in 1945 to about 98% in 1951. However, we in the Navy intend to remain prepared to bring medical facilities to the patients, where the exigencies of war may require it. There is no more satisfactory method of conveying a completely staffed and equipped general hospital from one part of the world to another than to float it in the form of a ship. Moreover, I will venture to warn once more against so naive an assumption that, because we have been able to fly helicopters and other aircraft almost *ad lib* in Korea, we could rely on the same practice against an enemy with air power comparable to our own.

Another advance has been the use by the Navy, in its medical service to the Marine Corps, of surgical teams. These units of three doctors and ten hospital corpsmen are moved about as needed to provide medical support at amphibious landings, aboard hospital ships, and in connection with Marine Corps field medical operations. These teams consist of a surgeon, his surgical assistant, and a physician anesthetist. They may at times contain specialists in neurology and psychiatry. They also have a representative distribution of enlisted medical technicians of special value in a given situation, including trained operating room technicians and laboratory men. The teams have special sets of equipment, including instruments, sterilizers, linens, and other surgical supplies.

The team members are kept in readiness, and their services may be utilized in base hospitals or other vantage points in the area. This permits them to become acquainted, to operate together, and to become organized

as an efficient unit. When needs for great amounts of surgery develop they are ready to fly or sail at short notice to points of action. They have served with the Marines during unusually heavy periods of activity, aboard hospital ships, as staffs for transports evacuating large numbers of casualties, and in other periods of heavy casualty incidence such as the Hungnam evacuation. Their readiness for action and adaptability for employment in hospitals during less active fighting periods not only enables better surgery for casualties but also prevents the waste of medical talent, such as sometimes occurred in former wars. These teams lessen the need for keeping various units unnecessarily staffed during quiet periods. At the peak of Marine Corps activity in Korea the Navy had 25 of these units in operation there.

The war on epidemic and infectious diseases in Korea has owed much to the use of floating epidemic disease control units. These are floating laboratories manned by appropriate personnel trained in the various aspects of preventive medicine and equipped to perform a disease prevention function. Tests to determine the nature of epidemic diseases are made close to the spot where they occur. Consequently, preventive and remedial action can be taken quickly to stop or deter the spread of epidemic diseases; and chemical or biological warfare agents can be analyzed quickly in the field to determine appropriate counter action. Without this mobility, specimens for analysis have to be sent to distant shore laboratories and preventive action based on laboratory tests is delayed.

The skilled and specially selected officers of the laboratories are trained to go ashore fully equipped, and to take measures to insure the safety of the fighting forces from diseases that lurk in the water or indigenous food supply, or those carried by flies, mosquitoes, rats, lice, and other living disease vectors. They can quickly analyze and measure the effectiveness of action taken. As mobile research laboratories, these units can go to many points otherwise extremely difficult to reach. The entomologists have made new and important observations of the disease carrying insects that produce typhus fever. They are busy with important projects to study and determine the effectiveness of various insecticides that are used primarily for elimination of this disease.

One innovation has been a one-man stretcher for use at the front. Several types, both with and without wheels, are being considered, and one or two models are actually on trial in Korea. Significant advances have been made in handling supplies. We have arranged special blocks of medical and surgical equipment that are packaged, shipped, and distributed in the field as units. These permit extremely rapid outfitting of various types of medical installations and also make possible rapid replacement of depleted supplies. The unusually quick build-up of medical supplies and facilities in the Far East in the Korean operation owed much to this device.

Finally, I think should be mentioned the development through joint medical research by the three services of a bullet resistant jacket that promises to reduce markedly the incidence and severity of wounds from small arms and shell fragments in the upper part of the body. The basic resistant material in these jackets is either doran (a "fiberglas" and plastic resin combination) or nylon, or a combination of the two. The major part of the work

in connection with this jacket has been carried out at the Navy's research laboratory on the Marine base at Camp Lejeune, N. C. (I might add that the Navy's laboratory at Camp Lejeune is the only facility of the armed services where work on the design and development of this jacket has taken place.)

The foregoing citations, I think, provide a fair index of the modern advances in military medicine. The net result of these advances and improvements is naturally that the kind of medical care that is being provided today for our armed services personnel is of a more effective and efficient brand than has ever hitherto been available. When an analytical view is taken of the concept of so all-important a matter as combat readiness, two basic elements appear to stand out. One of these is the doctrine of unification, and the other is the principle of flexibility. Flexibility has become the keynote of the current teaching in the military medical doctrine. Unification and flexibility currently constitute the burden of our theme.

We do not, I think, overestimate the importance of military medicine to national defense and defense of the free world. Lord Nelson, one of history's most distinguished admirals, said, "The great thing in all military service is health." Napoleon moreover observed that health is necessary in war and cannot be replaced by anything else. Considerable of our energies have been expended during the post World War II era opposing radical changes that have emanated from the inevitable "Monday morning quarterbacks." We do not consider, however, that these energies have been wasted. We intend to continue to endeavor to differentiate between fact and fantasy. We will continue to espouse measures to strengthen military medicine and to increase its service to the armed forces and to the civilian population.

AMERICAN BOARD OF MILITARY MEDICINE

We seek, for example, an American Board of Military Medicine that will give added recognition, dignity, and distinction to those who have seen combat service and have demonstrated outstanding qualifications in any of the several areas or categories peculiarly military in nature. In this connection I might mention that this year's Annual Achievement Award by the American Pharmaceutical Manufacturers' Association was shared jointly by the military departments for their contributions to research. At the time of the conferral of that award at a banquet in the Waldorf-Astoria in New York I was prompted, as I observed certain persons present at that banquet, to reflect on the validity of my view that service medicine is in itself a specialty.

Among its devotees are some highly defined experts. For example, at a banquet table in the group to which I refer sat a captain in the Medical Corps of the Navy who is the nation's and one of the world's foremost experts on submarine medicine. When one needs a doctor qualified to treat about 85% of the ills to which man is subject, that doctor may be found in almost any community; maybe he is just around the corner. But when a submarine is lying on the bottom of the ocean with a crew of human beings aboard, the kind of expert knowledge on which their salvation may well depend is possessed by an extremely small number of doctors. The doctor to whom I refer was largely responsible for the highly specialized scientific advances that made possible

the recovery of 33 men from the sunken *Squalus* off Portsmouth, N. H. in 1939. He, in fact, flew to the scene of that disaster and personally supervised the medical aspects of the rescue operations that were instituted upon that momentous occasion. He is a specialist without peer and should be so identified.

The Navy's policy will continue to be to provide special training to physicians, including conventional professional training, as well as special types such as that pertaining to the medical and military aspects of atomic energy and the medical implications of biological and chemical warfare. In times such as these the national security demands that all physicians have considerable knowledge of certain aspects of military medicine.

We will resist with all resoluteness possible creation of a single federal hospital system that includes the armed forces hospitals—a plan that has been advocated in certain quarters. We must retain our military hospitals under our own control in order that they be immediately responsive to military combat needs and in order that military patients may be immediately amenable to military transfer and assignment orders and to the various regulatory provisions under which a service organization operates.

At the same time we shall give such support as is within our province and appropriate to constructive plans for improving the program for medical care of dependents of service personnel. I believe that, in resisting inroads on our free medical system, we might well recall the words of the sage of Monticello, Thomas Jefferson: "I am not an advocate for frequent changes in laws and constitutions, but laws and constitutions must go hand

in hand with the progress of the human mind. As that becomes more developed, more enlightened, as new discoveries are made, new truths discovered, and manners and opinions change with the change of circumstances, institutions must advance also to keep pace with the times. We might as well require a man to wear still the coat which fitted him when a boy as civilized society to remain ever under the regimen of their barbarous ancestors."

We do not look toward sudden and revolutionary developments or changes. While change is essential to progress and progress is essential to life, a few things do not change. Birth and death are notable examples, and in between these two extremes is an abstract quality which, for want of a better term, we call human nature. This seems to change imperceptibly if at all, and so long as human nature remains what it is, certain measures will be necessary if we intend to maintain our position of dominance in the world's congress of nations.

In the military services, regardless of the department concerned, the "pitch" must always be towards and not away from preparedness for war; and if this is the pitch for the military services as a whole, it must, by a similar token, be the pitch for any component part of the services. And there is no component unit of the national defense establishment of greater importance in my estimation than that charged with the preservation and restoration of the most vital resource in the nation. I refer of course to health. And obviously the department upon which it devolves to protect this resource is the medical department.

Washington 25, D. C.

USE OF TRIETHYLENE MELAMINE IN TREATMENT OF LEUKEMIA AND LEUKOSARCOMA

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METHODS

Diagnosis in each instance was established by appropriate tests, including hematologic examinations, bone marrow aspiration, and lymph node biopsy. Almost all patients had been treated previously with such agents as roentgen rays, nitrogen mustard (NH₂), and urethane. Antibiotics and transfusions of blood were used as indicated. Patients were treated on both an inpatient and outpatient basis. Frequent observations of symptoms, physical findings, and blood cell counts were made.

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This study was aided by grants from the American Cancer Society (Massachusetts Division), the American Cancer Society, Inc., and the Lederle Laboratories. Dr. John Rueggesser of the medical staff of the Lederle Laboratories supplied the triethylene melamine used.

Our interest in the chemotherapy of leukemia and leukosarcoma,¹ which began with the use of nitrogen mustard in 1942,² led us to assay the value of an oral nitrogen mustard-like preparation, triethylene melamine (TEM), in the therapy of these disorders. The structural formula of this agent, chemically 2,4,6-triethylenimino-*s*-triazine, is shown in Figure 1. This agent has been shown to inhibit tumor growth in animals³ and is effective in prolonging the survival time of leukemic mice.⁴ Its chemotherapeutic activity is attributed to the ethylenimine ring,⁵ which is similar to the active hydrolysate of nitrogen mustard when this material is dissolved in water. The first clinical report of the use of this material was made by C. P. Rhoads in May, 1950, at a meeting of the Association of American Physicians. This preliminary report deals with the results of triethylene melamine therapy in 46 cases of Hodgkin's disease, leukemia, and related diseases.

The chemical, dispensed as 5 mg. scored tablets, was given orally in all instances. The ordinary dose in adults was 2.5 to 5 mg. Because of the extreme reactivity of the drug with organic molecules, it was given, as recommended by Rhoads and Karnofsky, on a fasting stomach with small amounts of water. Our procedure was to give the drug soon after the patient awoke in the morning and then to withhold breakfast for at least one hour. Some patients stated that reactions were lessened when they took the drug just before retiring at night.

REACTIONS TO TRIETHYLENE MELAMINE

Thiersch and Philips⁶ have reported the comparative toxic effects of nitrogen mustard and triethylene melamine in animals. Similar lesions were noted, namely, atrophy of all hematopoietic tissue and injury to intestinal epithelium. In our cases gastrointestinal upset was the most frequently encountered complaint. This usually occurred following the second or third dose of the drug, particularly if the full dose of 5 mg. was used and if the drug was given daily. Nausea and anorexia were commonly encountered, although vomiting was unusual. Reactions were almost always delayed, usually appearing about 6 to 8 hours after the drug was taken and usually disappearing within 24 hours. There was a great variability in individual reactivity to the drug. The percentage of patients showing each reaction is given in the following tabulation.

Anorexia	41.1
Nausea	55.8
Vomiting	29.4
Diarrhea	8.8
Hiccough	2.9
Retrosternal burning	2.9
No reaction	32.3

Depression of hematologic elements, particularly those of bone marrow origin, was regularly observed. The leukocytes and platelets were chiefly affected. The most marked leukopenic levels took place usually 20 days after therapy was begun; the most marked thrombocytopenic effect at 60 days. In some instances, marked reductions in various blood cell constituents were observed. In three patients with Hodgkin's disease pancytopenia developed, with thrombocyte levels under 50,000 per cubic millimeter. The cytopenia often persisted for as long as two or three months after cessation of therapy. Bone marrow studies in the patients in whom cytopenia developed revealed cellular hypoplasia, fatty replacement, and a great diminution in megakaryocytes.

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RESULTS IN HODGKIN'S DISEASE

Fifteen patients (Table 1) were treated, of whom 13 were in relapse. All patients had previously been treated with roentgen rays or nitrogen mustard. The patients in Cases 3 and 13 were in clinical remission when therapy was started. Cases 16 and 18 were examples of reticulum

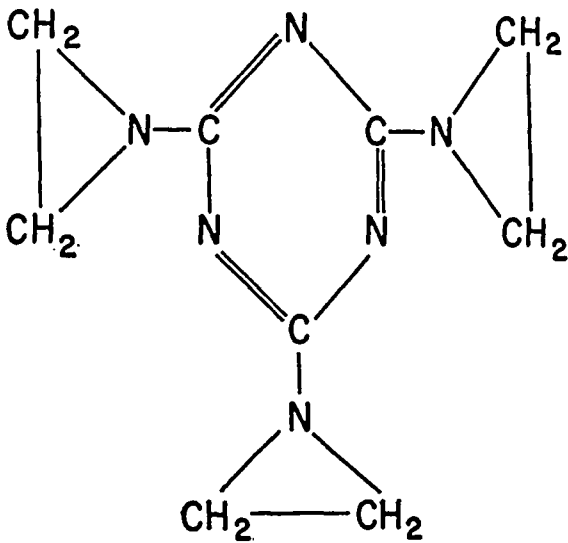


Fig. 1.—Structural formula of triethylene melamine (2,4,6-triethylenimino-s-triazine).

cell sarcoma, and the patient in Case 17 had lymphosarcoma. These latter three cases are included with the cases of Hodgkin's disease to facilitate grouping.

Dosages.—Two general factors influenced judgment as to the amount of drug to be given: the total leukocyte count prior to therapy and the severity of symptoms. Initial courses were given in a total dose of 10 to 30 mg. During this initial course the drug was usually given in 5 mg. doses on successive days. In recent cases the drug has been given more cautiously, with a dose of 2.5 mg. every day or every other day. After the initial course the patient was observed for two to four weeks, and the

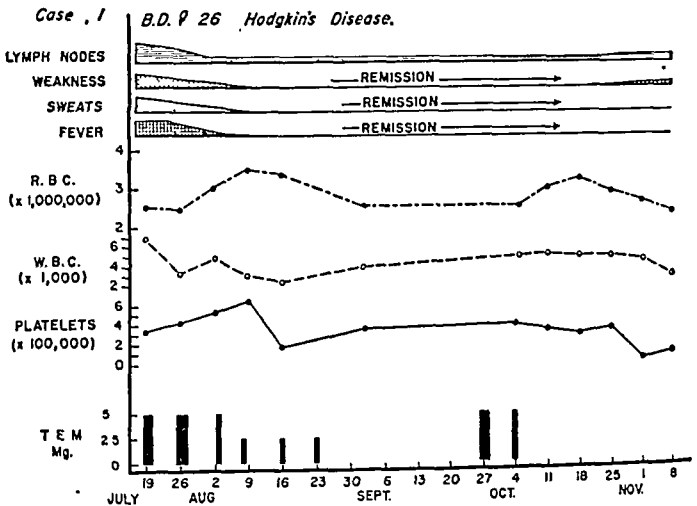


Fig. 2.—Course during treatment of woman with Hodgkin's disease.

drug was then continued in doses of 2.5 mg. twice a week or in a single dose of 2.5 to 5 mg. weekly. If the white blood cell count remained at levels of 5,000 or more and the platelet counts were normal, the drug was continued at weekly intervals. The two patients who were in remission when therapy was started were given weekly or biweekly doses of from 2.5 to 5 mg. At no

time during therapy was it necessary to discontinue the drug because of leukopenia or thrombocytopenia in these two cases.

Type and Duration of Response.—Complete remissions were observed in approximately 30% of the cases. These persisted for periods of 93 to 164 days. Approximately two-thirds of the patients showed definite but incomplete improvement. This partial response, which was both subjective and objective, was maintained for periods of 42 to 134 days. The patients in Cases 3 and 13 were in clinical remission prior to the start of triethylene melamine therapy and were still in remission 159 and 133 days after the start of therapy. Only one patient (Case 4) showed no effect from the drug. The therapeutic effect first became manifest in from 2 to 27 days and was usually heralded by relief of constitutional symptoms.

ing relief of constitutional symptoms was obtained, but a severe thrombocytopenia developed, with a platelet level of 32,000. The platelet count had risen to 115,000, 21 days after discontinuance of therapy. Bone marrow examination at the height of the thrombocytopenia showed hypocellularity and a complete lack of megakaryocytes.

In two patients complete disappearance of lymphadenopathy took place, while in five there was definite reduction in the size of the lymph nodes. The most striking reductions took place when the lymph nodes were greatly enlarged. In three patients there was complete subsidence of splenomegaly, but in a few cases there was no reduction in splenic size. Of four patients with generalized pruritus, two were completely relieved of this complaint in three to eight weeks. Partial relief was noted in the other patients. Nine patients complained of severe back pain, apparently due to intraspinal involvement by extension of the process from retroperitoneal

TABLE 1.—Analysis of Fifteen Cases of Hodgkin's Disease

Case	Age	Sex	Pretreatment Observations *							Course During and After Therapy										
			Constitutional Symptoms	Pruritus	Nodes	Spleen	Back Pain	RBC	WBC	Platelets	Total TEM,† Mg.	Observation Period, Days	Constitutional Symptoms	Pruritus	Nodes	Spleen	Back Pain	RBC	WBC	Platelets
1	26	F	+++++	0	++	+	0	2.52	6,950	352,000	50	111	+	0	+	+	0	2.67	4,400	115,200
2	22	F	+++++	0	++++	0	0	3.23	17,300	485,140	25	82	+	0	++	0	0	2.67	5,150	368,160
3	20	F	0	0	0	0	0	3.70	19,150	Normal	55	159	0	0	0	0	0	3.90	9,000	Normal
4	21	M	+++++	0	+	++++	+++++	4.25	7,300	Normal	35	136	+++++	0	+	++	++	3.80	2,950	Normal
5	57	F	+++	+++	++	++++	+++++	3.51	6,710	332,250	25	123	0	0	0	0	0	3.91	5,280	Normal
6	30	F	+++	+++++	++	+	0	3.01	14,550	411,555	45	142	0	+	+	+	0	3.47	19,000	326,180
7	32	M	+++	0	0	0	++	4.85	6,800	Normal	60	141	0	0	0	0	0	4.34	3,900	Normal
8	29	F	+++	0	+	+	0	3.41	15,700	832,040	40	108	++	+	+	+	0	2.82	9,000	226,800
9	48	M	++	+++	+	++	+++	4.30	11,000	495,000	65	82	0	++	+	0	++	3.99	8,500	391,200
10	40	M	+++	0	++	0	+++	4.25	10,600	350,000	75	174	+	0	+	0	+	3.25	7,550	Normal
11	25	M	+++	0	+	0	+++++	3.60	10,750	730,000	65	158	+++	0	+	+	++	2.68	1,700	26,800
12	43	F	+++	0	+	0	++	3.35	5,350	756,000	35	132	+	0	+	0	0	3.33	5,900	166,000
13	21	F	0	0	+	0	0	3.35	8,100	Normal	35	133	0	0	+	0	0	3.80	6,550	Normal
14	60	F	+++++	0	++++	++	+++++	3.30	5,650	403,500	35	173	+++	0	++++	0	+++++	3.50	2,950	Normal
15	31	M	+++++	0	0	0	++	3.32	16,000	346,122	95	145	+++++	0	0	+	++	2.82	11,450	50,760
16	39	F	+++	++	++	0	+++	4.80	5,750	Normal	70	130	+	+	0	0	+	3.90	4,000	Normal
17	65	M	+++	0	++++	++	0	4.17	5,850	372,000	20	97	+	0	++++	++	0	3.72	5,000	462,000
18	54	M	+++++	0	++++	0	++++	3.83	7,450	364,000	20	30	++	0	+	0	+	3.65	6,300	312,000

* The severity of symptoms was graded from 0 (not present) to ++++ (severe or generalized).

† TEM = triethylene melamine.

Effect of Triethylene Melamine on Clinical Manifestations.—Constitutional symptoms, such as weakness, malaise, lassitude, anorexia, night sweats, and fever, were the most prominent features of this particular series. Complete relief of these symptoms occurred in approximately one-third of the cases, and about two-thirds of the patients were relieved for variable lengths of time. An example of complete regression of constitutional symptoms is seen in the following case.

CASE 1.—Mrs. B. D. (Fig. 2), a 26-year-old woman, was given a diagnosis of Hodgkin's disease in 1948. Several courses of x-ray therapy were given with good results. In February, 1950, a course of nitrogen mustard resulted in a complete remission. However, in July, 1950, the patient again complained of fever, severe night sweats, weakness, and anorexia. At that time she showed marked pallor, temperature of 101.2 F, bilateral axillary adenopathy, and slight hepatosplenomegaly. The blood analysis showed 2,500,000 red cells, 6,950 white cells, and 350,000 platelets. On July 19 and 20 she was given 5 mg. of triethylene melamine. One week later she stated that she felt much better. Night sweats were no longer noted, and she was afebrile. Another 10 mg. was given on July 27 and 28. Following this, a complete remission was established, which lasted 93 days. Strik-

ing relief of constitutional symptoms was obtained, but a severe thrombocytopenia developed, with a platelet level of 32,000. The platelet count had risen to 115,000, 21 days after discontinuance of therapy. Bone marrow examination at the height of the thrombocytopenia showed hypocellularity and a complete lack of megakaryocytes.

Hematologic Changes.—The effect of triethylene melamine on the various constituents of the blood was analyzed after the initial course of therapy and again after maintenance therapy. Two to three weeks after beginning therapy, approximately one-fourth of the patients showed a rise in red blood cell count of 10.3% to 39.6%. A fall in red blood cell count of from 1.4% to 21.8% occurred in one-half the cases, whereas approximately one-fourth of the patients showed no change. After 20 to 95 mg. had been given over a period ranging from 30 to 174 days, one-third of the patients showed red blood cell counts that were higher after therapy than their pretreatment levels, while in about two-

thirds there was a slight drop. No unusual morphologic changes in the red blood cells took place.

A reduction in total white blood cell count took place in 83% of the cases. This fall in leukocyte count varied from 32% to 88% of the total white cell count and averaged 59%. Leukocyte counts began to fall within three to four days after therapy was begun, the lowest levels being obtained on about the 20th day after the first dose. Individual responses were quite variable, and it was impossible to predict the degree of fall in any patient. Leukopenia usually disappeared in about two to three weeks after cessation of therapy. The fall in white blood cell count was due to an absolute reduction in granulocytes. A tendency toward hypersegmentation of the polymorphonuclear cells was noted at times.

A reduction in platelet count was observed in 50% of the cases. This was usually of slight degree and transient in nature, once the drug was discontinued. Reductions in platelet counts were not usually observed until after at least a month of therapy. In three patients undergoing

higher dosage schedules were used in these cases than in the group with Hodgkin's disease, but there was a wider range of dosage because of the high white blood cell counts.

Effect of Triethylene Melamine on Clinical Manifestations.—Weakness, anorexia, and weight loss were the outstanding symptoms in these cases. Subjective improvement was dramatic in five cases. Case 4 (Fig. 3) may be cited in summary as an example of an excellent temporary therapeutic result.

CASE 4.—R. J., aged 31, had been known to have chronic granulocytic leukemia since 1947. From then until March, 1950, he had received courses of x-ray therapy over the spleen at about six-month intervals. In July, 1950, he was again in relapse, complaining of weakness, anorexia, and marked weight loss. Further x-ray therapy was thought inadvisable by the radiologist. Examination revealed a pale, sallow, emaciated man. The entire left half of the abdomen was deeply pigmented, indurated, and scarred from the intensive x-ray therapy. Both the liver and the spleen were felt 2 fingerbreadths below their respective costal margins. There was anemia, marked leukocytosis

TABLE 2.—Analysis of Eight Cases

Case	Sex and Age	Pretreatment Observations *				Clinical Symptoms	Treatment			
		Red Blood Cells	White Blood Cells	Platelets	Spleen		Initial Dosage T E M †	Lowest White Count After Initial Course	Total T E M, Mg.	Observation Period, Days
1	M 54	4.07	84,800	500,000	+++	++	15 mg. in 5 days	9,900 in 10 days	25	35
2	M 26	4.15	12,850	400,000	++++	+++	10 mg. in 2 weeks	8,300 in 20 days	25	68
3	F 49	3.80	168,000	500,000	++++	++++	30 mg. in 6 days	3,700 in 17 days	60	115
4	M 27	2.74	180,000	8,000,000	++	++++	20 mg. in 4 days	3,950 in 40 days	35	101
5	M 55	3.61	120,000	477,500	+++	+++	25 mg. in 5 days	33,350 in 13 days	50	50
6	F 37	3.23	52,000	675,070	+	+++	10 mg. in 2 days	51,000 in 7 days	25	50
7	M 55	3.92	24,600	400,000	++	++	10 mg. in 6 days	20,000 in 18 days	65	112
8	M 31	3.33	130,000	666,600	+++	+++	25 mg. in 5 days	44,000 in 22 days	9.75	167

* The severity of symptoms was graded from 0 (not present) to ++++ (severe). † T E M = triethylene melamine.

long-term therapy thrombocytopenia developed, with platelet counts of 50,000 or under. One patient (Case 1) had a platelet level of 32,000 after receiving 50 mg. of triethylene melamine during a period of 111 days. Another patient (Case 15) showed a platelet level of 50,700 after receiving 95 mg. during a period of 145 days. In the patient in Case 11 marked thrombocytopenia developed following administration of 65 mg. of triethylene melamine. His platelet level was 26,800 after five months of therapy. In this case platelet depression was first noted after four months of therapy, and the platelets continued to fall even after therapy was discontinued.

CHRONIC GRANULOCYTIC (MYELOGENOUS) LEUKEMIA

Eight patients with chronic granulocytic leukemia (Table 2) were treated with triethylene melamine. All patients had been treated previously with roentgen rays, urethane, or radioactive phosphorus, with the exception of the patient in Case 8. Complete remissions, as evidenced by a fall in white blood cell counts to normal and alleviation of all symptoms, occurred in three cases and were maintained for 35 to 107 days. Three patients showed improvement clinically and hematologically, while two patients were in no way benefited. Slightly

(150,000 white blood cells) and thrombocytosis (with 8,000,000 to 12,000,000 platelets per cubic millimeter). The patient was given 20 mg. of triethylene melamine over a four-day period. Seven days later the platelet count had fallen from 8,000,000 to 1,000,000. At this time the patient felt better than he had in several years and was completely asymptomatic. With further maintenance dosage of triethylene melamine, hematologic relapse of slight degree occurred but was controlled by increasing the dose of the drug. The patient was asymptomatic six months after beginning therapy and showed normal white blood cell counts and only slight elevation of platelet counts.

Two patients showed complete disappearance of splenomegaly. One of these patients (Case 1) had received x-ray therapy over the spleen with no decrease in splenic size. Four months later the spleen was felt 6 fingerbreadths below the left costal margin. One month after triethylene melamine therapy was instituted the spleen was palpable one fingerbreadth below the costal margin. The patient in Case 8 (Fig. 4) showed complete disappearance of splenomegaly four months after the start of triethylene melamine therapy. Five patients showed no reduction in size of the spleen, although the leukocyte levels were reduced in three.

Hematologic Changes.—Within two to three weeks after the start of therapy, five patients had rises in the red cell counts of from 4.5% to 20.4%. Falls in red cell

counts were noted in three patients, two being terminal cases. After protracted therapy four patients had higher red blood cell counts than at the beginning of treatment. A fall in white blood cell count was observed in every patient. Dramatic reductions in white cell counts were noted in five instances. White cell counts often began to fall by the third treatment day, and the lowest leukocyte levels following doses of 10 to 30 mg. were observed on the 10th to 40th days. One patient (Case 8) was an exception and showed a delayed type of response. This patient's course of therapy and response is seen in Figure 4. It was not always possible to maintain a normal white cell count, as in Cases 3 and 5, in which an excellent initial response could not be maintained, despite continued therapy. The reduction in primitive cells always paralleled the fall in total white cell count, and only when leukopenic levels were reached did metamyelocytes and myelocytes completely disappear. Five patients had no essential change in platelet counts during treatment. The severe thrombocytosis in Case 4 was

nomegaly, and the differential count of the white cells was essentially normal. At the first indication of a drop in leukocyte level below 5,000, or in the platelet count below 100,000, therapy with triethylene melamine was discontinued temporarily, until normal counts were re-established.

ACUTE LEUKEMIA

Six adult patients with acute leukemia were treated with triethylene melamine. Five patients had acute "myelomonocytic" leukemia, and one had the acute granulocytic form. Triethylene melamine was administered in doses of 5 mg. daily for a total of 20 to 40 mg. Results were consistently poor. A fall in total white cell count was often noted, but there was no improvement in the severe anemia or thrombocytopenia. Serial bone marrow studies were made in several cases. The basic picture of unusual marrow cellularity was not changed by therapy. Following is a report of the one patient with acute lymphocytic leukemia treated with triethylene melamine after other treatment had failed.

of Chronic Granulocytic Leukemia

Present Status

Red Blood Cells	White Blood Cells	Platelets	Spleen	Clinical Symptoms	Comment
4.00	7,400	400,000	+	0	Taking 2.5 mg. every 2 weeks; has had complete remission
2.67	26,600	26,600	++++	++++	Died from tuberculosis and myeloblastic crisis; no response to T E M
2.85	347,200	95,200	++++	++++	T E M given for 86 days then stopped; remission for about 80 days; died 115 days post-treatment
3.52	67,000	8,000,000	0	0	Excellent response; dose reduced; white cell count rising
3.96	112,000	400,000	+++	+	Initial response but not maintained; x-ray given with a fall in white blood cells to normal
3.62	30,350	500,000	+++	++	Poor response to T E M; x-ray then given; little response
4.05	14,600	400,000	+++	+	Definite clinical and hematological improvement; still receiving weekly doses of T E M
4.45	11,450	500,000	0	0	Receiving T E M, 2.5 mg. 2 times a week; clinical and hematological remission

dramatically reduced. Thrombocytopenia developed in two patients in myeloblastic crisis during treatment, but the fall in platelets was probably part of the course of their disease.

CHRONIC LYMPHOCYTIC LEUKEMIA

Early in these studies suitable cases of chronic lymphocytic leukemia were not available. More recently, however, we have used triethylene melamine in 10 cases of this disease. Good to excellent results were obtained in seven patients. In these, the white blood cell counts were reduced to normal levels concurrently with striking reductions in lymph node size and splenic mass. There was a rather marked variability in individual response, but, in the cases showing the most favorable effects, the patients became clinically and hematologically normal for long periods of time, provided that small doses of the drug were given regularly. Treatment was usually begun in a dosage of 2.5 mg. every other day for four to six doses, after which it was given in the same dosage at intervals of 5 to 15 days. The attempt was made in each case to maintain the white cell count at levels of between 6,000 to 10,000 per cubic millimeter. At these levels, there was usually no palpable lymphadenopathy or sple-

This patient was a 2½-year-old girl who had had several previous remissions following "aminopterin" (4-amino folic acid) and corticotropin (ACTH) therapy. Because of lack of further response to these agents, triethylene melamine was given, in a dose of 2.5 mg. At the start of therapy a pronounced enlargement of the parotid and submaxillary glands was present. Within three days the lymphadenopathy had almost completely regressed. Forty-eight hours after the initial dose the white count had fallen from 35,200 to 3,700, and on the fifth post-treatment day only 130 leukocytes per cubic millimeter were found. In 20 days the white cell count had returned to normal levels but then continued to rise, and lymphadenopathy returned. A dose of 1.25 mg. was then given, with no effect, and the patient died two months after the initial dose of triethylene melamine.

COMMENT

Triethylene melamine appears to be effective in a variety of malignant disorders of the leukocytic tissues. This drug seems more versatile than the other chemotherapeutic agents. For example, nitrogen mustard is effective in Hodgkin's disease but only slightly effective in the leukemias. Folic acid antagonists are of value only in the acute leukemias, especially those of the lymphocytic variety. Urethane is most effective in chronic granulocytic leukemia and multiple myeloma. Triethylene melamine, however, has well-defined effects in chronic

granulocytic leukemia, chronic lymphocytic leukemia, Hodgkin's disease, and in some cases of lymphosarcoma. The largest group of patients treated with this material had Hodgkin's disease. The disease in these patients was far-advanced and generalized. Like nitrogen mustard, triethylene melamine has distinct value in the treatment

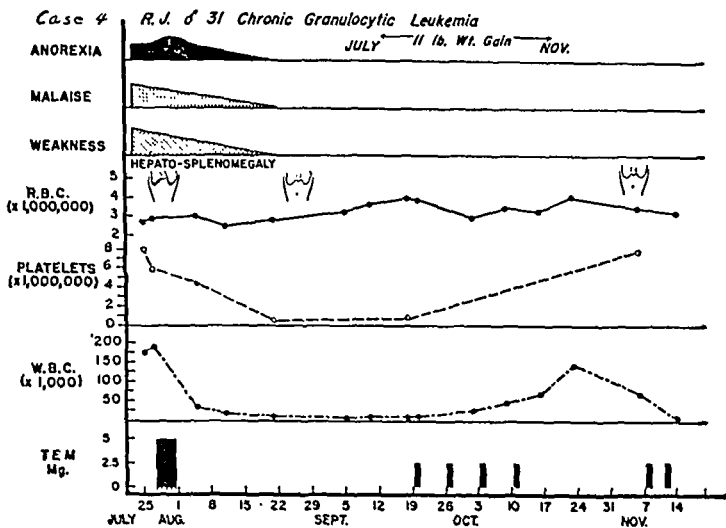


Fig. 3.—Course during treatment of a man with chronic granulocytic leukemia, with an excellent therapeutic result.

of this late stage of Hodgkin's disease when radioresistance has developed or the process has become generalized, with many systemic symptoms, such as weight loss, itching, fever, and night sweats. Improvement in constitutional symptoms was noted in almost all patients treated, and complete clinical remissions were seen in several cases.

The availability of an oral preparation as potent as triethylene melamine represents a great advance in the treatment of Hodgkin's disease. This in itself is the greatest advantage that triethylene melamine has over nitrogen mustard. The severe gastrointestinal reactions seen with nitrogen mustard are a great disadvantage. Reactions from triethylene melamine are much less frequent and far less severe than with mustard therapy. The reactions seen with nitrogen mustard have made attempts at maintenance therapy almost impossible and have made hospitalization necessary. This is usually not essential with triethylene melamine therapy. In 1949, one of us (W. D.)² reported complete remission rates of 34.3% with nitrogen mustard therapy in generalized Hodgkin's disease. Remission rates with triethylene melamine are comparable. Although this group of patients is smaller than the series treated with nitrogen mustard, complete therapeutic failures seem less frequent with triethylene melamine. In addition, the remissions induced by triethylene melamine appear to be of longer duration than with nitrogen mustard.

In our earlier studies all patients were given maintenance therapy in the hope of keeping the process in check once an adequate therapeutic response was seen. Several patients who were in clinical remission were given 2.5 to 5 mg. of the drug at weekly or biweekly intervals, and they continued in sustained remission for four-month and five-month periods. Although such a situation is difficult to evaluate, it is probable that this was more than coincidence, since the average patient with advanced Hodgkin's disease does not remain

clinically asymptomatic for such extended periods. However, several patients undergoing prolonged and continuous therapy have shown evidence of well-defined marrow hypoplasia and blood cytopenia, notably thrombocytopenia. Other patients have had relapses while undergoing triethylene melamine therapy, which indicates that the drug is by no means as valuable for maintenance therapy as we had at first hoped. Chiefly because of the development of cytopenia, it appears probable that triethylene melamine given continuously may be a hazardous method of treatment in most cases of Hodgkin's disease. It is probably best, therefore, to give the drug in an initial course of 15 to 20 mg. and then in divided doses of 2.5 to 5 mg. This dose appears to be optimum in cases of Hodgkin's disease, lymphosarcoma, and reticulum cell sarcoma. Some effect should be noted within a two-week period. If after four weeks no beneficial effect has been observed, another 5 to 10 mg. can be given, providing leukocyte counts and platelet levels are normal. This therapeutic approach is similar to the plan of treatment with nitrogen mustard. If maintenance therapy is still desired, it should be given in doses of 2.5 mg. once weekly or biweekly. At the first sign of a well-defined reduction in platelets, triethylene melamine should be discontinued.

Our experience with the use of triethylene melamine in lymphosarcoma and reticulum cell sarcoma has been limited. Regression of lymphadenopathy in lymphosarcoma is often striking, and constitutional symptoms may be greatly relieved. In two patients requiring frequent thoracentesis, the rapid reaccumulation of pleural fluid seemed to be checked with triethylene melamine. One patient has been maintained with triethylene melamine therapy for 130 days. In these highly malignant diseases, although the basic disease process may not be materially altered, the rapidity of the process seems to be distinctly slowed.

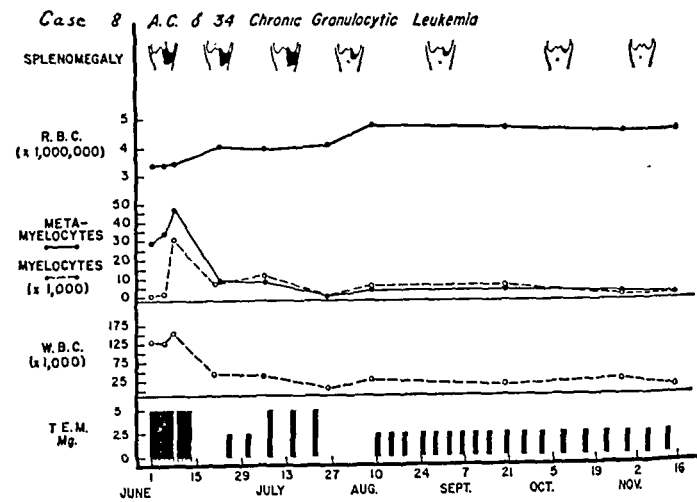


Fig. 4.—Course during treatment of a man with chronic granulocytic leukemia, showing delayed response.

Good results were usually obtained in the treatment of chronic granulocytic leukemia. Almost all cases are well advanced. Control of the proliferative process was observed in six cases, with dramatic reductions in white blood cell counts, reduction of splenomegaly, alleviation of severe constitutional symptoms, and relief of the anemia. Remissions were maintained for as long as 107

days. In two cases the drug had no effect. Our experience with triethylene melamine in previously untreated patients has been limited to one patient, in whom a remission was induced and maintained. More experience is needed as regards the effect of this drug in early cases of chronic granulocytic leukemia. We still feel that x-ray therapy over splenic fields is the treatment of choice in early cases. For maintenance or with the development of x-ray resistance, triethylene melamine may be effective. Bone marrow depression at the alarming levels seen in Hodgkin's disease was not observed, probably because the margin of safety is much greater in these cases with very hypercellular marrows and often pathologically high platelet counts. Maintenance therapy is completely practical, particularly when frequent white blood cell counts can be obtained and the dosage regulated either by the physician or occasionally, as in one of our cases, by the patient himself, who was able to obtain weekly white cell counts from a cooperative laboratory. Another patient regulated his own dosage by learning to do his own white cell counts.

Early results of triethylene melamine therapy in chronic lymphocytic leukemia are highly encouraging. Hematologic remissions were observed in two patients who had become resistant to x-ray therapy. Reduction in white blood cell counts, lymphadenopathy, and splenomegaly were noted in most cases. The drug should not be used in this disease when platelet counts are already distinctly reduced, since it may lower the platelet counts to even more critical levels, with the result that hemorrhage may then be added to an already difficult situation.

Results in acute leukemia, especially of the granulocytic and monocytic variety, have been discouraging. The terminal myeloblastic crisis as seen in cases of chronic granulocytic leukemia was also not affected by triethylene melamine. One child with acute lymphocytic leukemia showed a brief but effective response. Our experience with monocytic leukemia of the subacute variety is also limited to a single case. This patient had good results with continuous therapy, although there was no basic change in the peripheral blood or bone marrow.

Because of the striking myelosuppressive effects of triethylene melamine, we were led to use it in polycythemia vera, which is characterized by panmyelosis and pancytosis. The early results of therapy have been encouraging. In several patients with thrombocythemia with platelet levels often above 5,000,000 and with the history of hemorrhagic manifestations and recurrent thrombophlebitic episodes, the use of triethylene melamine has also been very effective. In one patient showing platelet levels of about 4,500,000, a reduction in platelets to 1,000,000 took place after four weeks of therapy, with abrupt cessation of the thrombotic episodes and a decided subjective improvement. The results obtained in such cases are comparable to those obtained with radioactive phosphorus and possess the added advantage that the patient is not subjected to the possible deleterious effects of x-irradiation.

SUMMARY AND CONCLUSIONS

Forty-six patients with leukemia, leukosarcoma and related diseases were treated with triethylene melamine, a nitrogen mustard-like preparation for oral administration. The activity of this agent is attributed to its ethylenimine ring, which is similar to the active hydrolysate of nitrogen mustard. Reactions to triethylene melamine were for the most part gastrointestinal, with nausea in about one-half and vomiting in about one-third of the cases. Reactions were usually delayed, appearing about eight hours after administration of the drug. Slight to moderate depression of hematologic elements, particularly those of bone marrow origin, was regularly observed with the dosage given.

Triethylene melamine is often an effective agent in the treatment of generalized and radioresistant cases of Hodgkin's disease. Remissions occurred in 30% of the patients treated and lasted for as long as 164 days. The drug was given in divided doses of 2.5 to 5 mg. in an initial course of 20 to 30 mg. Triethylene melamine appears to be as effective as nitrogen mustard in the treatment of Hodgkin's disease. Its greatest advantage over nitrogen mustard is the fact that it can be given by the oral route. There is a decidedly lower incidence of gastrointestinal reactions. When a rapid therapeutic effect is required, as in marked mediastinal involvement with dyspnea, intravenous administration of nitrogen mustard is preferable.

Patients with lymphosarcoma and reticulum cell sarcoma have shown temporary improvement with triethylene melamine therapy. Marked improvement has been noted in cases of chronic granulocytic leukemia, with striking reductions in white cell count and diminution in splenomegaly. Complete remissions have been maintained for as long as 107 days. Maintenance therapy in doses of 2.5 mg. a week is recommended in the treatment of this disease, once white cell counts have been reduced to normal. Early results in chronic lymphocytic leukemia indicate that the drug may have its most striking effects in this disease. Several patients have been maintained for long periods of time in complete clinical and hematologic remission. The course of acute leukemia in adults was unaltered by triethylene melamine. One case of acute lymphocytic leukemia in a child showed striking regression of lymphadenopathy. This effect was only temporary, the patient eventually succumbing to the disease.

Hypoplasia of the bone marrow was observed with long-continued administration of triethylene melamine in Hodgkin's disease. Frequent blood cell counts, including estimations of the platelets, are essential when using this chemotherapeutic agent. Triethylene melamine appears to be a highly active chemotherapeutic agent having a broad spectrum of effectiveness against various leukocytic proliferative diseases. In addition, its general myelosuppressive activity may make it a valuable agent in the treatment of polycythemia vera and thrombocythemia.

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VOLUNTARY MULTIPLE HEALTH TESTS

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and

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Since October, 1945, over 1,000,000 residents of Georgia have voluntarily taken multiple health tests. The most outstanding and valuable feature of Georgia's voluntary program is the close harmony between the health departments and the practicing medical and dental professions. The state and county medical and dental societies sponsor the program. Preliminary reports were presented in 1946, at the Southern Medical Association meeting in Miami,¹ and in 1947, at the Forty-Third Annual Meeting of the National Tuberculosis Association in San Francisco.² At first, the program consisted principally of tests for tuberculosis and syphilis. In 1946, about 40,000 persons received oral and dental examinations, in addition to other tests. In 1949, the Anthrone blood sugar method was found to be adaptable to mass screening procedures.³ In 1950, blood sugar and hemoglobin tests and height and weight determinations were added to the battery of tests in the greater Atlanta Survey, and the chest roentgenograms were read for cardiovascular conditions, malignant disease, and other chest diseases as well as for tuberculosis. The tests were not considered substitutes for complete physical examinations but as scientific tests for specific conditions. Various other tests have been considered but not included in the Georgia program, because of technical or other difficulties; for example, blood pressure determinations were rejected as being medically unsound for persons under the mental strain of mass survey psychology.

From April 4 to June 30, 1950, a total of 235,000 persons voluntarily reported for testing in the greater Atlanta survey. This was the most comprehensive survey, not only in the number of persons tested in a short period of time but also in the number and variety of tests offered each person. For this reason, the Atlanta survey is reported herewith in some detail. The cost was about \$1.31 per person tested, the most expensive in our experience. Since the time of the Atlanta survey, costs have averaged about \$1.00 per person, but the dental examination and the height and weight determinations have been omitted.

Fourteen testing stations were operated in Atlanta during the first part of the testing period; toward the end, as few as seven were in operation. A few of the units were in permanent locations, but most were of a mobile nature. Stations were set up in large downtown department stores, the lobbies of office buildings, in churches, schools, community centers, and in industrial locations.

Portable units sometimes remained in one place for several weeks; at other times, they were moved daily. Selection of conveniently located stations was a "must" in mass testing. Each station unit was geared to examine from 80 to 100 persons per hour. The staffing of the stations did not require constant attendance of a physician. Dental examinations were made by a dentist at each station, and nurses and technicians administered the other tests. However, all units had professional supervision.

Mass testing has been referred to as a "scattergun" method of case finding; however, "pinpoint" case finding was accomplished in the Atlanta survey in one section where it was thought that the prevalence of disease would be abnormally high.⁴

Atlanta has a four block section of densely populated negro dwellings and shops that might well be called a "casbah." No empty, available indoor space could be found to set up a testing unit in this area; therefore, an open air station was established beneath a viaduct that runs through the center of the section. Here, a different, flamboyant, method of publicity for the program was used. In the five weeks in which the station was operated, 16,000 persons voluntarily submitted to the tests. Later, the wisdom of concentrated effort in this neighborhood was proved. The tuberculosis rate was 0.83% in the "casbah," as compared with 0.77% in the population at large. The cardiovascular rate was 1.36% compared with 1.1% in other sections. The syphilis reactor rate was about 33% or four and one-half times as high as in other areas. The following information refers to the Atlanta survey, except where noted otherwise.

TUBERCULOSIS

Seventy millimeter photofluorographic units were used for making the initial chest roentgenogram. Persons were recalled to a diagnostic center if the initial film was unsatisfactory or showed evidence of tuberculosis or other chest disease. Further tests were then made, including a tuberculin skin test and roentgenogram on a 14 by 17 in. film when indicated. All films showing suspicious cardiovascular changes were reviewed by a board of cardiologists. Of 213,488 persons tested, tuberculosis was diagnosed in 1,648 (0.77%). Of these, 287 were classified as active, 794 as questionably active, and 567 as inactive. Among the 1,648 persons who were designated as tuberculous, 1,347 (81.5%) did not know of the presence of this condition. In addition, 699 cases were classified as suspicious, and 1,738 examinations were not completed.

CARDIOVASCULAR CONDITIONS

The physicians making the initial readings of the 70 mm. roentgenograms were requested to be alert for cardiovascular abnormalities. All films in which a possible abnormality was noted were referred to special cardiac consultants for further study. On the recommendation of these consultants, nearly 2,400 persons were referred to

From the Georgia Department of Public Health (Drs. Petrie and Bowdoin) and the Department of Medicine, Emory University (Dr. McLoughlin).

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3. Petz, R. H., and Petrie, L. M.: The Anthrone Blood Sugar Method Applied to Diabetes Case Finding in a Multiple Screening Program, Pub. Health Rep. 65: 1709 (Dec. 22) 1950.

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their private physicians, with a transcript of the preliminary findings, as having definite or suspected cardiovascular disease.

OTHER CHEST DISEASES

The roentgenograms were also studied for chest disease other than tuberculous or cardiovascular in nature, and 666 persons were referred to their private physicians. This included 52 cases tentatively diagnosed as pneumoconiosis.

SEROLOGIC TEST FOR SYPHILIS

For the serologic test for syphilis, all screening specimens were submitted to the venereal disease research laboratory, where the laboratory's rapid slide flocculation test was used. Persons with a positive or weakly positive reaction were requested to report to a central diagnostic center for further examination. If indicated, a second serology specimen was submitted to the state survey serology laboratory. These specimens were tested by both the venereal disease research laboratory technique and the Kahn technique. Both of these tests were submitted to physicians in the diagnostic center. Of 228,024 specimens submitted, 22,348 (9.8%) gave positive reactions. Of the persons with positive reactions, 2,245 had new or previously unknown cases of syphilis and 9,426 were patients with known cases, who resumed treatment; thus, a total of 11,671 patients with syphilis were referred for treatment. Of these, 88 cases were diagnosed as primary or secondary lesions, 135 were diagnosed as cardiovascular syphilis, 1,166 were diagnosed as neurosyphilis, and 483 were diagnosed as congenital syphilis. These figures represent the cases found directly by the survey. Contact investigation was integrated with the syphilis case finding in the survey. Trained and experienced communicable disease investigators interviewed all patients. They interpreted the findings to the patients and arranged for treatment, either by private physicians or at the Alto Medical Center. All infectious or potentially infectious patients were interviewed before they were referred for treatment. Investigation of the named contacts turned up more than half of the 197 cases of primary and secondary syphilis that were discovered. Contact investigation must be an integral part of any mass testing in which syphilis case finding is included.

HEMOGLOBIN

For hemoglobin determinations, the copper sulfate specific gravity test was used. After consultation with the advisory committee of the medical association, it was decided that men with hemoglobin concentrations below 11 gm. per 100 cc. and women with concentrations below 10 gm. per 100 cc. were to be referred to their private physicians for further study. Of 180,128 tests tabulated, 9,749 (5.4%) gave abnormal results.

ORAL AND DENTAL EXAMINATIONS

The dental examinations included extraoral inspection of the head, face, and neck as well as oral examination. The examining dentists carefully checked enamel dystrophies, the condition of the mucous membranes, periodontal diseases, carious conditions, missing teeth, replacements, and occlusions. Of the persons examined,

21% were referred to a dentist for immediate treatment, and another 49.3% were referred for more extensive examinations. If possible infection or neoplastic disease was found, the patients were referred to a diagnostic center, where a specialist in oral diseases made further examinations. There were 1,300 persons (0.6%) who were told to report for additional examination. Of the 708 who reported, 166 had extra oral lesions and 442 had neoplastic and/or precancerous lesions. Letters of referral to be taken to their private physicians and dentists were given to 258 persons. Unfortunately, however, few biopsy reports were received. Nine cases were termed definitely cancerous. More complete follow-ups would probably increase this figure considerably.

BLOOD SUGAR

Early in 1949, the late Dr. James Edgar Paullin brought to the attention of the state board of health the idea that a diabetes detection drive should be incorporated into the county-wide voluntary screening programs. Tests of urine specimens to determine abnormalities of sugar metabolism were studied; however, results of experimental work performed in the division of industrial hygiene laboratory indicated that blood sugar determination was the method of choice for the detection of abnormal carbohydrate metabolism. Further study led to the adoption of the Anthrone method³ as the most efficient, consistent, and reliable test for blood sugar as well as the most suited to our particular problem. The basic concepts of this program were presented to the medical association and approved.⁵ Atlanta conducted the first blood sugar screening program on such a large scale. It was a pioneering program. As with any new program, and especially one on such a large scale, certain technical difficulties were encountered, most of which have since been overcome.

Statistics of the Atlanta survey show that 3.3% of the population examined had an abnormally high blood sugar level. Confirmatory blood sugar tolerance tests were not done on these persons as part of the survey; they were referred for confirmatory tests to their own physicians. Probably, one-third of them would have been eliminated as diabetic suspects had confirmatory blood sugar tolerance tests been done. It was found that 7% of the population were 25% or more overweight.

Our statistics of subsequent surveys will be broken down in terms of color and sex, in 10 year age groups, showing completed blood sugar tests, including confirmatory blood sugar tolerance tests when indicated. One group of six counties tested in 1951 included 43,543 persons, of whom 55 were previously known diabetics, 449 had previously unknown abnormal blood sugar metabolism, and an additional 169 were classified as borderline cases.

This makes a total detection rate for confirmed or suspected cases of 1.55% of the total population examined; only 8% of these persons stated that they were previously known diabetics, although it is our opinion that the majority of them could be given the diagnosis of diabetes mellitus, if they had adequate medical care. It must be

remembered that the screening procedure does not diagnose diabetes nor does it detect known diabetics, who, as result of adequate treatment, have normal blood sugar levels, unless they volunteer the information that they have the disease. It is important to note that in 21% of the abnormal and borderline cases, there was no sugar in the urine at any time during the glucose tolerance test. This apparently confirms the impression that blood sugar testing is more effective than urinalysis as a diabetes detection screen test.

COMMENT

An overwhelming vote of confidence is being given by both physicians and laymen to the multiphasic health testing surveys in Georgia. All economic and social groups greet the program enthusiastically. The 1,000,000 persons voluntarily tested to date represent more than 60% of the entire adult population of the areas in which the surveys have been conducted. The surveys, however, are perhaps only a passing phase that will lead to the eventual offering of such tests by the local health departments as a routine service to all citizens on a periodic basis, perhaps annually or, in special cases, more frequently. Smillie⁶ suggested that the diagnostic facilities now used in mass health testing should be developed as a source to which the physician, with his comprehensive knowledge of the whole person, could refer his patient but should not be available to the general public, except through such referral. We agree that this proposal would be the best, if through it, each of the 155 million citizens of the United States could have a physical examination; however, it is also estimated by Smillie that "900 out of 1,000 persons tested under multiphasic screening programs are not under medical supervision." This is apparently supported by our findings that 81.5% of the tuberculosis patients found in the Atlanta survey had not been previously known to have the disease, and only 8% of those suspected of having diabetes in our 1951 surveys stated that they knew of their condition. Our screening tests swamp the physicians with more applicants from previously unsupervised group than the physicians can handle with ease. Many of these applicants are potential patients, whose screening tests indicate suspicion of disease. If the medical profession is going to advocate annual examinations, where needed, it should cooperate with the public health profession in scientific case finding, as has been done in Georgia. The primary responsibility for this type of preventive service rests on the practicing physicians in cooperation with the health departments. Neither can do a good job without the other.

Surveys were found to be most effective in health education. What was learned, was learned by doing. Education has been defined as "the transmission of knowledge from one with authority, to one who is eager to learn, who has the ability to understand, and who is motivated to a change in action." Here, there was transmission of knowledge from the health department as the administrative agency, from one with authority, the medical and dental professions, and motivated change in action in the form of the voluntary application of 1,000,000 persons for the tests. No method of health education, other than the multiphasic screening survey, has been demonstrated that will effectively educate as high a percentage of the

previously apathetic and medically unsupervised public. Half the adult population of the state has been motivated to take the tests. The routine report form sent to each person, including the ones whose tests were negative, carries this message: "We wish to make it plain these tests do not in any way take the place of a physical examination by your family physician. We recommend that in the interest of good health you should see your family doctor at least once a year for a complete physical examination." Large numbers of previously unsupervised persons heed this advice and visit their own physicians.

SUMMARY

This report is based on voluntary multiple health tests that have been performed on more than 1,000,000 persons in Georgia during the past six years. Almost all these persons have been tested by chest roentgenograms and by syphilis serology. Over 300,000 persons in the past year and a half have been given blood tests for anemia and for abnormalities of carbohydrate metabolism. Smaller numbers have had oral and dental inspections by dentists and height and weight determinations. All evidence points to the fact that at least in Georgia, with the specific tests enumerated here, multiphasic health test surveys of more than half the entire adult population of the state can be done in a manner mutually profitable and acceptable to all. Both patient and physician profit from early case finding when the patient is still capable of self-support and is not a burden to his family or the state.

The possibility of successful surveys may still be debated, but in Georgia they are an accomplished fact. Such success would never have been possible in Georgia had there not been the background of many years of understanding and harmony between the practicing physicians and their professional brothers in the field of public health. In this same spirit of harmony, our medical and public health professions propose to continue working together toward solutions of our many common and pressing problems. There is no doubt that the multiphasic screening surveys are giving both professional and lay persons more insight into these problems.

6. Smillie, W. G.: "Multiphasic" Screening Tests, *J. A. M. A.* 145: 1254 (April 21) 1951.

Appendicitis Mortality.—Marked progress continues to be made in the control of appendicitis mortality. Among the Industrial policyholders of the Metropolitan Life Insurance Company, the death rate from this cause has been reduced more than 60% in the past five years and by 80% in the past decade. . . . The death rate from the disease has dropped to less than 1 per 100,000 at a number of age groups among both white males and white females. The rapid decrease in the death rate from appendicitis in recent years is undoubtedly attributable in large part to the widespread use of the antibiotics against peritonitis, a complication which is responsible for most of the deaths charged to appendicitis. General improvement in medical care and operative techniques have also played their part in reducing the hazard of surgery. It seems likely, too, that with the spread of health education an increasing proportion of patients seek treatment early, before complications arise. The story of appendicitis is a proud chapter in the recent history of American medicine. Yet there is still room for further improvement. In 1950 the disease took well over 3,000 lives in the general population of the United States.—Appendicitis Death Rate Still Decreasing, *Statistical Bulletin, Metropolitan Life Insurance Company*, December, 1951.

CLINICAL NOTES

SPONTANEOUS HEALING OF SICKLE CELL ANEMIA ULCER IN PREGNANCY

Theodore Cornbleet, M.D., Chicago

Observers long have been aware of the influence of pregnancy on various diseases, such as rheumatoid arthritis and some skin disorders. Costello,¹ Crawford and Leeper,² and Hollander and Vogel³ have summed up a good deal known about this influence of gestation on cutaneous disease. Recently, I showed that diseases of the apocrine sweat glands (hidradenitis suppurativa and Fox-Fordyce disease) improve spontaneously during pregnancy.⁴ The ulcers of sickle cell anemia, too, may apparently be modified by pregnancy.

One of the commonest clinical characteristics of sickle cell anemia is ulceration of the legs. It tends to be chronic and probably results from trauma and the tendency to thrombosis in this disease. Either the ulcers or their scars are said⁵ to be present in three out of every four adults with sickle cell anemia. They are uncommon in children but appear during adolescence. They are found commonly about the ankles and then next most frequently on the lower third of the leg anteriorly, unilaterally or bilaterally. There may be only one ulcer or several, with some healed by atrophic, glossy, depigmented scars. The ulcers may be punched out or shallow with grayish, granular bases and scanty discharges, at times of pus. The edges are raised, irregular, and hyperpigmented. The lesions are tender. The ulcers heal slowly but later may remain indefinitely, in spite of treatment. The lesions need to be distinguished from syphilis, ecthyma, erythema induratum, and tuberculosis colliquativa.

There is disagreement about the effects of sickle cell anemia on pregnancy. Abortion is said to be usual, if conception takes place at all.⁶ The anemia, too, is made worse by pregnancy.⁷ Anderson and Busby,⁸ cited by Greenhill,⁹ reviewed the literature and found 33 reported cases in which there was a total of 73 pregnancies. The maternal death rate was 21%, and abortions totaled 19.1%. Fifty of the 59 viable infants remained alive. In contrast to this, in Anderson and Busby's 11 cases the women all survived. They concluded that pregnancy does not necessarily augur a poor prognosis in the presence of sickle cell anemia. Probably nutrition, the kind of antepartum and postpartum care, and other factors are decisive in the outcome. Edington¹⁰ reports the autopsy findings in two cases of sudden death in African primigravidas. The findings were strikingly similar and probably were predetermined by environment and other factors.

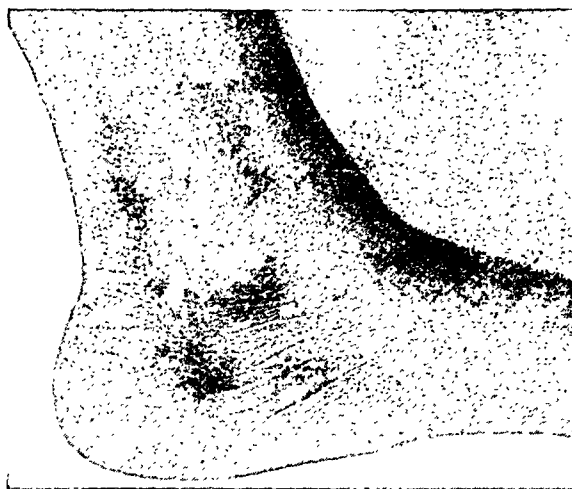
Because of the difference of opinion on the influence of pregnancy on the health of the subject with sickle cell anemia, it seems desirable to report observations on one of my patients.

REPORT OF A CASE

R. B., a Negro woman, 20, was observed because of ulceration of the ankle. She showed a number of old scars on the legs, representing healed ulcers. The ulcer had raised, irregular edges

and a granular, grayish base exuding a seropus with a somewhat offensive odor. The lesion was about 6 cm. in diameter and at places 0.5 cm. deep. There was tenderness and some pain. The leg showed no varicosities. With numerous systemic and local measures, there was little progress toward healing during two and a half years. Rest in bed and aureomycin ointment did the most, but even so there was no substantial progress.

With sponge dressings healing began to take place rapidly. Then it was discovered that the patient was pregnant—her first time—whereupon all treatment for the ulcer was discontinued, but improvement continued until it healed completely. There was nothing noteworthy about the pregnancy except that there were no crises. Prior to pregnancy she had crises with abdominal pain, rapid depression of hemoglobin and erythrocytes and with exhaustion and collapse at intervals of four to six months. She went to term, and parturition was uncomplicated, with rapid restoration to her prepregnant state. Despite the high point of her hemoglobin and red cell count—74% and 3,800,000—the ulcer was beginning to reappear at its same site three months after delivery of a baby boy. Despite diligent care, the ulcer was soon of its previous size. During pregnancy and the healing of the ulcer, there was no change in the sickling capacity of the red cells. Other laboratory data were not noteworthy.



Healed sickle cell anemia ulcer during pregnancy.

COMMENT

Judging by this patient's experience, one would have to agree with Anderson and Busby that sickle cell anemia is not the dire threat in pregnancy that others have found it. Nevertheless, obstetricians would recommend the extreme precautions against complications taken in the case reported herein. The patient had close prenatal observation and every care in the delivery room as well as

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1. Costello, M. J.: Eruptions of Pregnancy, *New York State J. Med.* 41: 849, 1941.

2. Crawford, G. M., and Leeper, R. W.: *Diseases of Skin in Pregnancy*, Arch. Dermat. & Syph. 61: 753, 1950.

3. Hollander, L., and Vogel, H. R.: Notes Concerning Some of the More Frequent Skin Diseases Occurring During Pregnancy, *Pennsylvania M. J.* 48: 454, 1945.

4. Cornbleet, T.: Apocrine Gland Diseases and Pregnancy, *Arch. Derm. & Syph.*, to be published.

5. Sturgis, C. C.: *Hematology*, Springfield, Ill., Charles C Thomas, 1948.

6. Kobak, A. J.; Stein, P. J., and Daro, A. F.: Sickle-Cell Anemia in Pregnancy: Review of Literature and Report of 6 Cases, *Am. J. Obst. & Gynec.* 41: 811, 1941.

7. Soderman, W. A., and Burch, G. E.: *Pregnancy in Active Sickle Cell Anemia*, *New Orleans M. & S. J.* 90: 156, 1937.

8. Anderson, G. W., and Busby, T.: *Sickle Cell Anemia and Pregnancy*, *Am. J. Obst. & Gynec.* 58: 75, 1949.

9. De Lee, J. B., and Greenhill, J. P.: *Principles and Practice of Obstetrics*, Philadelphia, W. B. Saunders Company, 1947.

10. Edington, G. M.: Sickle-Cell Crisis in Pregnancy: Two Autopsy Reports, *Tr. Roy. Soc. Trop. Med. & Hyg.* 44: 559, 1951.

postpartum. Modern obstetrical care and good nutrition unquestionably contributed to the good result.

There was no change in the sickling trait during pregnancy to explain the healing of the ulcer. The hemoglobin and cell count were both improved, however, which may explain the healing. However, both had not changed materially at the time the scar broke down again, three months postpartum.

1819 W. Polk St.

PRIMARY ENTEROCOCCIC (STREPTOCOCCUS FAECALIS) MENINGITIS

CURE EFFECTED WITH COMBINED PENICILLIN AND STREPTOMYCIN THERAPY

A. Allen Goldbloom, M.D.

Martin L. Goldfarb, M.D.

and

Milton Schlachman, M.D., New York

The enterococci comprise a group of hemolytic and nonhemolytic streptococci which are members of the nonpathogenic Lancefield group D. These organisms are usually saprophytic inhabitants of the gastrointestinal tract. They have, however, been found in many human diseases, such as endocarditis, intestinal infections, abdominal infections due to injury of the intestinal tract, infections of war wounds, and infections of the urinary tract. Occasionally they cause acute suppurative otitis media in children. Indeed, enterococci are more frequently isolated from clinical sources other than the respiratory tract, than any other *Streptococcus*.

Enterococci are a rare source of acute purulent meningitis. The majority of reported cases are secondary to a known focus of infection. We have been able to collect

ly five cases of primary enterococcic meningitis from the literature. It is the purpose of this communication to add a sixth case of primary enterococcic meningitis, to discuss the treatment of this disease, and briefly to review the literature.

REPORT OF A CASE

G. B., a 17-year-old white boy, was admitted to the hospital on Feb. 4, 1951. Being irrational, the patient was unable to give his own history. His mother stated that on the morning of admission the patient complained of persistent headaches and that he vomited several times. For two days prior to admission the patient had had a nonproductive cough. There had been no previous cough, chest pain, or hemoptysis. The past history was noncontributory.

Physical examination revealed a lethargic boy who thrashed about and resisted every effort to examine him. The temperature was 101 F, pulse rate 60, blood pressure 120/60, and respirations 28. The pupils were round, regular, and equal and reacted to light. The fundi could not be visualized because of the patient's resistance, nor could accommodation be tested. The ears, nose, and throat appeared normal. The pharynx could not be

visualized because of lack of cooperation. There was marked nuchal rigidity of the neck and slight tender right anterior adenopathy. There was no cardiac enlargement. A systolic murmur was heard throughout the precordium, loudest at the apex. Regular sinus rhythm was present. The lungs were clear to percussion and auscultation. The abdomen was soft. There was no tenderness, and no organ edges or masses were palpable. Brudzinski and Kernig signs were positive. There was no Babinski sign. Deep tendon reflexes were normally active throughout. There were no skin rashes nor petechiae.

Laboratory Data.—A spinal tap was performed immediately on admission. Dynamics could not be evaluated because of the patient's resistance. The fluid obtained was turbid and contained 16,000 white cells per cubic millimeter; 50% were polymorphonuclear leukocytes and 50% were round cells and were presumed to be lymphocytes. No organisms were noted on the stained smear (Gram stain). The blood chemistry showed fasting blood sugar 137 mg. per 100 cc., urea nitrogen 9.3 mg. per 100 cc., and a negative Wassermann reaction. A chest x-ray showed increased hilar markings with increased markings extending to both bases. The electrocardiogram showed normal sinus rhythm.

Clinical Course.—A clinical diagnosis of meningococcic meningitis was made, and treatment with aqueous penicillin, 200,000 units every two hours, and sodium sulfadiazine, 5 gm. in 500 cc. of sixth-molar lactate intravenously daily, was immediately started. On this regimen of daily intravenous sulfadiazine and 2,400,000 units of penicillin, there was slight improvement clinically. On the fourth hospital day the sulfadiazine dosage was changed to 1 gm. orally every four hours. His fever and meningeal signs persisted. A second lumbar puncture on the fifth hospital day revealed an initial pressure of 300 mm. of water, and clear fluid which contained 450 white blood cells per cubic millimeter, consisting of both polymorphonuclear leukocytes and lymphocytes. On the sixth hospital day the patient's condition deteriorated as evident by severe headache and marked meningeal signs. On the eighth hospital day the penicillin was increased to 400,000 units every two hours. The following day slight symptomatic improvement was noticed despite the persistence of fever. On the 10th hospital day, however, the patient again had excruciating headache. Physical examination at this time revealed the persistence of slight nuchal rigidity, bilateral Kernig sign, and persistent fever, with no papilledema.

Because of the poor therapeutic response, the original diagnosis of meningococcic meningitis was abandoned. On the 10th hospital day a spinal tap revealed an initial pressure of 160 mm. of water, with rapid rise to 320 mm. under jugular pressure and a rapid fall on release. A clear fluid with 900 white cells per cubic millimeter, all lymphocytes, was obtained. No organisms were seen on smear. On the 11th hospital day 3 gm. of streptomycin given intramuscularly was added to the above therapeutic regimen. On the 12th hospital day penicillin, 12,000,000 units daily, was administered.

The above spinal fluid cultures were reported as showing *Enterococcus* (*Streptococcus faecalis*), insensitive to penicillin, aureomycin, and chloramphenicol, but sensitive to streptomycin. From the time that 12 million units of penicillin and 3 gm. of streptomycin were administered daily, the patient promptly became afebrile and showed rapid clinical improvement. The patient was discharged cured. Unfortunately follow-up lumbar puncture was refused.

COMMENT

We have collected 26 cases of enterococcic (*Streptococcus faecalis*) meningitis from the literature. Five of these are examples of acute primary enterococcic meningitis with no known focus of infection; three cases reported are incomplete as to the presence or absence of a portal of entry and are hence considered questionable. Seventeen cases have been reported in the literature as examples of enterococcic meningitis secondary to a known focus of infection; two cases secondary to tonsillar infection; three cases produced by lumbar punc-

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The bibliographic references, which have been omitted from THE JOURNAL because of lack of space, are included in the authors' reprints.

ture; six cases resulting from otitis media; two cases produced by bronchopulmonary infection; three cases following gastrointestinal tract infection; and one case following puerperal sepsis. One case, reported as secondary in origin, listed no primary focus. Thus enterococcal meningitis is an unusual disease which is, in the majority of recorded cases, secondary to a definite purulent focus or to introduction of the organism into the spinal fluid during a lumbar puncture.

As in other enterococcal infections, the treatment of enterococcal meningitis poses a formidable challenge, since the organism is usually resistant to sulfadiazine, penicillin, and streptomycin. Experience with subacute bacterial endocarditis due to *Enterococcus* has shown that the treatment of choice consists of massive doses of penicillin combined with streptomycin. Our case demonstrated that the same principle applies to the therapy of enterococcal meningitis.

Initially a clinical diagnosis of meningococcal meningitis was made; treatment naturally was oriented toward the use of sulfadiazine combined with fairly large doses of penicillin. When lack of response to sulfadiazine and increasing doses of penicillin was noticed, the original diagnosis of meningococcal meningitis became untenable. Streptomycin and massive doses of penicillin were employed to combat the as yet unknown organism, with clinical recovery. Spinal fluid cultures revealed the presence of *Enterococcus* (*Streptococcus faecalis*) prior to therapy and during the initial inadequate therapy, sensitive *in vitro* only to streptomycin.

The data on the newer antibiotics are as yet too meager to permit one to determine their place in the treatment of enterococcal meningitis, although in two cases the disease responded to aureomycin.

SUMMARY

The sixth case of primary enterococcal (*Streptococcus faecalis*) meningitis is reported. The patient was cured with combined streptomycin and massive doses of penicillin. It is recommended that any patient with meningitis not responding to ordinary therapy be given a trial of such combined therapy of the order of 12 million units of penicillin and of 3 gm. of streptomycin daily, since the disease may be due to an unusual organism, as herein mentioned.

2 E. 95th St. (28) (Dr. Goldbloom).

Medical Teachers.—By a curious distortion of values capacity for teaching is more likely to be a handicap than a help to a young person who aspires to be a good clinical teacher. Perhaps this paradox results from failure to take seriously the main responsibility of a clinical chief, which is teaching. As medical teachers are chosen today with the eye averted upon volume (and not necessarily quality) of published papers, it is accidental if superior talent for teaching adorns the odd assortment of characteristics demanded of medical department heads. No one has dared confront the curriculum head on and align it with the vast and incomprehensible array of new facts not yet codified in any sensible order. Always it is add another appendage. Unless a revival of integration permits wholesale pruning and sensible grafting, the academic tree, overburdened with miscellaneous fruit, will fall of its own weight and spoil the harvest.—W. B. Bean, M.D., *A Testament of Duty: Some Strictures on Moral Responsibilities in Clinical Research*, *Journal of Laboratory and Clinical Medicine*, January, 1952.

COUNCIL ON PHARMACY AND CHEMISTRY

REPORT TO THE COUNCIL

The Council has authorized publication of the following report from its Committee on Research.

ROBERT T. STORMONT, M.D., *Secretary.*

The Committee on Research, through its Subcommittee on Steroids and Cancer, is sponsoring a collaborative study on steroids and mammary cancer. Reports summarizing this work have been published (Estrogens and Androgens in Mammary Cancer, Report to the Council on Pharmacy and Chemistry, J. A. M. A. 140:1214 [Aug. 13] 1949. Proceedings of the First Conference on Steroid Hormones and Mammary Cancer, Chicago, A. M. A. [April] 1949. Current Status of Hormone Therapy of Advanced Mammary Cancer, Report to the Council on Pharmacy and Chemistry, J. A. M. A. 146:471 [June 2] 1951).

In the following report, the conclusions expressed are those of the authors and final conclusions of the Subcommittee must await evaluation of the studies now in progress.

PAUL L. WERMER, M.D., *Secretary.*

MINERAL AND PROTEIN METABOLISM IN OSTEOLYTIC METASTASES

Daniel Laszlo, M.D., Cyril A. Schulman, M.D., Judith Bellin, M.S., Estelle D. Gottesman, B.S., and

Albert Schilling, M.D., New York

In recent years, considerable progress has been made in the early diagnosis and management of cancer. Experimental data have been accumulated on the effects of hormone and chemotherapeutic agents which may prevent or possibly retard tumor growth in human beings and animals. To judge whether such agents have prevented tumor development or inhibited its rate of growth, careful standardization of experimental conditions is essential.

Standardization of experimental conditions in human neoplasms is difficult. A more thorough knowledge of the spontaneously occurring variations in the course of the disease is of paramount importance. The beneficial effects of therapeutic agents and their mode of action, as well as the mechanism of toxic side-reactions can be established only by assessing the range of variations in the natural course of the disease.

The skeletal system in man is frequently affected by cancer, resulting in major complaints and disability. Freid and Goldberg¹ found osseous metastases in 75% of patients with metastatic breast carcinoma. Garland and co-workers² state that skeletal metastases occur in a high percentage of cases of advanced mammary cancer and may constitute the leading source of distress and disability from that disease since pain, immobilization, fractures, severe anemia, and hypercalcemia may accompany skeletal involvement.

Standardization and evaluation of spontaneous variations in human disease have been achieved most successfully under the controlled conditions of a metabolic study. In diseases involving

From the Division of Neoplastic Diseases, Montefiore Hospital.

This project has been supported in part by a grant from the American Cancer Society and by a grant from the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service.

1. Freid, J. R., and Goldberg, H.: Treatment of Metastases from Cancer of the Breast, *Am. J. Roentgenol.* 63: 312 (March) 1950.

2. Garland, L. H.; Baker, M.; Picard, W. H., Jr., and Sisson, M. A.: The Comparative Effectiveness of Roentgen and Steroid Hormone Therapy in Mammary Cancer Metastatic to Bone, Report to the Council on Pharmacy and Chemistry, J. A. M. A. 144: 997 (Nov. 18) 1950.

the skeletal system, studies of calcium, phosphorus, and nitrogen metabolism have been helpful in defining the nature of the disease process and in evaluating the effect of therapy. Such studies have demonstrated that immobilization of normal human subjects results in protein and mineral catabolism.³ Similar effects were seen following traumatic fracture.⁴ The negative mineral balance in osteoporosis has been studied and the anabolic effects of androgen and estrogen demonstrated.⁵

It would be expected that similar studies of patients with skeletal metastases could also serve as a controlled experiment. Data obtained in such studies could be compared with those found in benign bone diseases, and the specificity of therapy investigated. This line of investigation was further stimulated by the advent of palliative hormonal therapy for metastatic malignancies, which furnished a great deal of primarily clinical data.

The Committee on Research of the American Medical Association has undertaken to coordinate these investigations,⁶ and data have been obtained on several hundred cases of breast cancer which were treated with varying doses of androgen and estrogen. In the course of these cooperative studies a number of important questions were raised, several answered, and a few left in abeyance. It is hoped that investigations such as this one will aid in clarifying a few of these points.

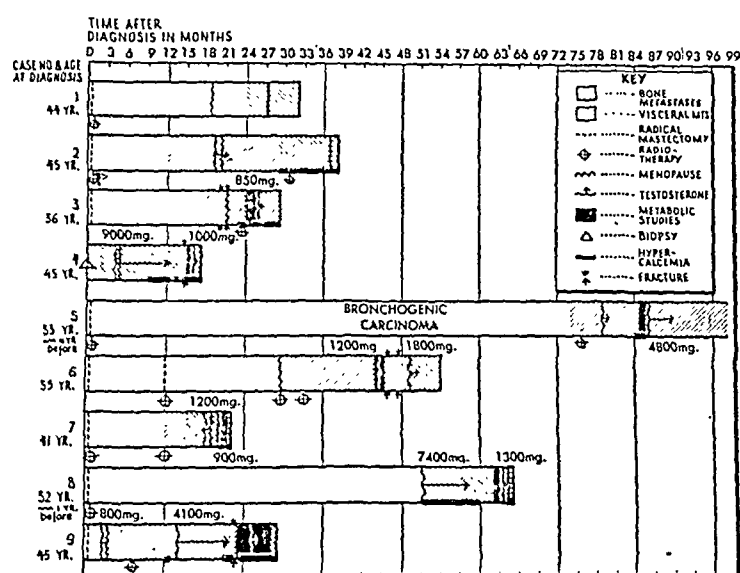


Fig. 1.—Schematic representation of the histories on nine patients with breast carcinoma from the time of diagnosis until death. Case 1 had visceral metastases but no bone involvement; the other patients all had extensive osteolytic metastases.

There are a few reports in the literature on the effects of cancer upon metabolism of bone. Albright and Reifenstein⁷ investigated a case of hypernephroma with bone metastases in which the chemical and metabolic findings were similar to those of hyperparathyroidism. Kennedy, Tibbetts, Nathanson and Aub⁸ have reported a metabolic investigation of patients with advanced carcinoma of the breast. Aub, Tibbetts, and Nathanson⁹ investigated the metabolism of patients with prostatic carcinoma. Members of this study group have presented pre-

liminary reports on the metabolic characteristics of metastatic breast and prostatic carcinoma.¹⁰

This report deals with the clinical and metabolic behavior of skeletal cancer involvement in man. Its aim is to group the malignant bone diseases into organic units; to analyze the influence of these progressive diseases upon metabolism; to study the spontaneous fluctuations, the progress, and complications of these diseases and, based on this data, to attempt to evaluate therapeutic agents.

METABOLIC STUDIES OF OSTEOLYTIC METASTASES

Eight patients with extensive osteolytic metastases secondary to breast carcinoma were studied. A ninth patient with metastatic breast carcinoma and no demonstrable bone involvement was included in the series as control.

The cancer histories of the patients are represented in figure 1. The diagnoses were established histologically and the clinical course was closely followed by frequent routine laboratory tests and serial roentgenograms.

The duration of metabolic studies in this series ranged from 6 to 155 days and averaged 50.3 days. The metabolic routine was similar to that described by Reifenstein, Albright, and Wells.¹¹ The patients were given a low calcium diet, approximately 0.15 gm. of calcium and 0.6 gm. of phosphorus per day. The caloric requirements of each patient were considered. The actual calcium, phosphorus, and nitrogen content of the food was determined by chemical analysis of dietary aliquots every six days. Urine and stools were collected daily and analyzed for calcium, phosphorus, and nitrogen. The balances were determined for each six day period by comparing the intake and the total excretion.

As a control for the patients with osteolytic metastases, the ninth patient, case 1, was included in the series as a patient without demonstrable bone involvement. When she was 44 years of age, this patient underwent a left radical mastectomy and postoperative radiotherapy for anaplastic carcinoma of the breast with axillary metastases. Spontaneous menopause occurred 19 months later. She remained well for two years, and then axillary nodes were noted and a right pleural effusion yielded tumor cells. Roentgenograms indicated pulmonary and pleural metastases, but no bone changes were apparent. Metabolic studies were performed for three periods of six days each; two control periods followed by a period during which calcium gluconate was administered orally to bring the daily calcium intake to 0.555 gm. The data are summarized in table 1. The patient was in a state of positive nitrogen balance throughout the period of study. The urinary calcium excretion was within normal limits and the calcium balance close to equilibrium, even on a low calcium intake. When the calcium intake was increased in the third period, bringing the dietary calcium-phosphorus ratio to the "physiologic" range of 1:1, the urinary calcium excretion remained the same. The fecal calcium increased, but to less than the increment in intake, resulting in positive calcium balance. During the period of calcium gluconate supplementation, the urinary phosphorus decreased, the fecal phosphorus increased, and the balance was less positive than in the preceding control periods. The significance of the theoretical and unaccounted phosphorus balance will be discussed later. This patient, who did not have bone involvement, exhibited normal calcium balance with positive nitrogen and phosphorus balances.

EFFECT OF OSTEOLYTIC METASTASES ON METABOLISM

In contrast to the normal mineral metabolism of a patient without bone metastases is the mineral catabolism seen in the patients with osteolytic metastases. Figure 2 illustrates a case of breast carcinoma with extensive metastases. The patient, case 2, a 48-year-old single woman, had three years previously undergone a left radical mastectomy followed by radiotherapy for infiltrating duct carcinoma with axillary metastases. Bone metastases were first noted one year later. Testosterone therapy was then given resulting in a cessation of menses and temporary symptomatic improvement. However, later in the course of therapy, the symptoms became more acute, hypercalcemia developed, and roentgenograms revealed progression of extensive osteolytic metastases. After testosterone was discontinued, the symptoms disappeared, but they later recurred as did the hyper-

3. Deitrick, J. E.; Whedon, G. D., and Shorr, E.: Effects of Immobilization Upon Various Metabolic and Physiologic Functions of Normal Men, *Am. J. Med.* 4: 3 (Jan.) 1948.

4. Howard, J. E.; Parson, W., and Bigham, R. S., Jr.: Studies on Patients Convalescent from Fracture: The Urinary Excretion of Calcium and Phosphorus, *Bull. Johns Hopkins Hosp.* 77: 291 (Oct.) 1945.

5. Adams, M.; Boothby, W. M., and Snell, A. M.: Metabolic Studies in Osteoporosis, *Am. J. Physiol.* 114: 383 (Jan.) 1936. Reifenstein, E. C., Jr., and Albright, F.: The Metabolic Effects of Steroid Hormones in Osteoporosis, *J. Clin. Investigation* 26: 24 (Jan.) 1947.

6. Proceedings of the First Conference on Steroid Hormones and Mammary Cancer: The Therapeutic Trials Committee of the Council on Pharmacy and Chemistry of the American Medical Association, Chicago, 1949.

7. Albright, F., and Reifenstein, E. C., Jr.: *The Parathyroid Glands and Metabolic Bone Diseases: Selected Studies*, Baltimore, Williams and Wilkins Co., 1948.

8. Kennedy, B. J.; Tibbetts, D. M.; Nathanson, I. T., and Aub, J. C.: Chemical and Systemic Changes in Patients with Advanced Carcinoma of the Breast Following Hormonal Therapy and Castration, *Cancer Res.* 9: 551 (Sept.) 1949.

calcinemia. Radiotherapy was administered to the pelvis with partial relief of pain, but the hypercalcemia persisted. At the time of the metabolic studies, the patient had not received hormonal therapy for 18 months or radiotherapy for six months. Figure 2 illustrates that in spite of a moderately positive nitrogen balance, the calcium and phosphorus balances are negative. The negativity of the calcium balance is accounted for mainly by the hypercalcinuria that averages 0.395 gm. per day.

Table 2 summarizes the data of 30 metabolic periods in nine patients. It is then subdivided into two groups: (1) 12 periods for three patients (cases 1, 8, and 9) who exhibited normal urinary excretion, and (2) 18 periods for the other six who were hypercalcinuric (urinary calcium excretion exceeding 0.15 gm. per day).

The nitrogen balances ranged from 3 gm. retained to 2 gm. lost and averaged 0.403 gm. retained per day. This indicates that even advanced breast cancer patients with extensive metastases can be maintained in a state of protein balance.

The average nitrogen balances of the normal calcinuria group and of the hypercalcinuria group did not differ significantly. There are, however, major differences in the calcium and phosphorus metabolism of the two groups.

averaged 0.354 gm. per day. The fecal calcium excretion was elevated to a lesser degree, averaging 0.21 gm. per day. This was greater than the calcium intake, indicating that endogenous calcium is also excreted by the bowel. The phosphorus excretion in this group was greater than in normal subjects and resulted in negative phosphorus balance. Most of the excess phosphorus was excreted in the urine, resulting in hyperphosphaturia. The significance of the unaccounted phosphorus retention will be discussed subsequently.

The data derived from the hypercalcinuric group indicate that marked osteolysis is characterized metabolically by excessive urinary calcium excretion, inversion of the urinary-to-fecal calcium ratio, negative calcium and phosphorus balance, and hyperphosphaturia. When the degree of osteolysis and negative mineral balances becomes excessive, hypercalcemia ensues. The mechanism of hypercalcemia in patients with osteolysis will be discussed later.

It is apparent that the difference in the calcium and phosphorus balances between the two groups was caused mainly by the increment in urinary calcium and phosphorus. Evaluating this increment, an increase of 0.32 gm. in urinary calcium excretion and an increase of 0.154 gm. in urinary phosphorus is

TABLE 1.—Nitrogen, Calcium, and Phosphorus Balances in an Untreated Patient with Breast Carcinoma, Visceral Metastases, But No Bone Involvement

Period	No. Days	Wt., Kg.	Urino (Vol.), ml./24 Hr.	Nitrogen, Mg./24 Hr.				Calcium, Mg./24 Hr.				Phosphorus, Mg./24 Hr.				
				Intake	Urino	Stool	Balance	Intake	Urino	Stool	Balance	Intake	Urino	Stool	Actual	Theoretical
1*	6	53.9	806	8,300	5,366	833	+2,101	131	31	125	-25	651	219	68	+304	+129
2*	6	56.1	1,160	6,733	4,433	350	+1,950	153	49	127	-23	665	234	80	+351	+119
			Average	7,517	4,900	592	+2,025	142	40	126	-24	658	237	74	+357	+124
3	6	55.4	1,179	5,016	4,133	533	+350	555	42	239	+274	508	142	133	+233	+147

* The patient (case 1) received a low calcium diet in periods 1 and 2, which was supplemented by oral administration of calcium gluconate in period 3.

TABLE 2.—Average Metabolic Data of Nine Patients with Breast Cancer on a Low Calcium Diet Who Received No Treatment

Case	Periods	Nitrogen, Mg./Day, Balance	Calcium, Mg./Day			Phosphorus, Mg./Day			
			Urino	Stool	Balance	Urino	Stool	Balance	Unaccounted for
1, 2, 3, 4, 5, 6, 7, 8, 9.....	30	+403	226	196	-294	324	176	-11	+96
1, 8, 9*.....	12	+315	31	175	-91	231	154	+101	+121
2, 3, 4, 5, 6, 7.....	18	+462	354	210	-428	385	185	-84	+82

* These patients exhibited normal calcinuria.

† These patients were hypercalcinuric (urinary calcium excretion exceeding 150 mg. per day).

The normal calcinuria group on a low calcium diet exhibited a calcium balance that was slightly negative. As in normal subjects, most of the calcium was excreted through the bowel. The urinary calcium excretion averaged 34 mg. per day, which is at the lowest limit of normal. The phosphorus balances of this group were slightly positive, with most of the phosphorus being excreted in the urine.

The normal calcinuria data are derived from three patients. One patient did not have osseous metastases (case 1). The other two patients (cases 8 and 9) had extensive osteolytic metastases. Both of these patients had suffered from previous bouts of hypercalcemia from which they recovered. In this phase, they exhibited normal serum calcium values and normal calcium and phosphorus balances. They later exhibited hypercalcinuria, negative calcium and phosphorus balances, hypercalcemia, and hyperphosphaturia. They illustrate that patients with extensive osteolytic metastases may exhibit, metabolically as well as clinically, a fluctuating course of remission and exacerbation. The disease progresses in waves of osteolysis and attempt at repair. This will be described later in more detail.¹²

The other six patients had extensive osteolytic metastases. All were hypercalcinuric and three were hypercalcemic in this phase. In spite of negative calcium and phosphorus balances, the average nitrogen balance was positive. The calcium balance was negative, averaging -0.428 gm. per day. Hypercalcinuria

found between the two groups. This ratio of urinary calcium to phosphorus increment is 2.1:1, which closely approximates the ratio of calcium to phosphorus present in bone. This indicates that in osteolytic metastases the excess calcium and phosphorus resulting from bone breakdown is excreted mainly in the urine.

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12. Schilling, A.; Schulman, C. A.; Bellin, J.; Gottesman, E. D., and Laszlo, D.: A Metabolic Study of the Effects of Testosterone on Patients with Osteolytic Metastases, Particularly in Breast Carcinoma, *J. A. M. A.*, to be published.

RELATIONSHIP OF SERUM CALCIUM TO URINARY CALCIUM

It has just been demonstrated that active osteolysis is characterized by hypercalcinuria and hyperphosphaturia with the excess urinary calcium and phosphorus present in the ratio corresponding to the mineral content of bone. Since there is increased excretion of minerals, a comparison of the serum and urinary levels of calcium and phosphorus in these patients is indicated.

Figure 3 illustrates the urinary calcium excretions and the serum calcium levels of the nine patients during metabolic study. A close relationship is evident between the fluctuations of urinary calcium and serum calcium levels. Major fluctuations in urinary calcium excretion are accompanied by signs and symptoms of critical progression or temporary improvement of the patient.

The eight patients with osteolytic metastases (cases 2 to 9) all exhibited hypercalcinuria in excess of 0.15 gm. per day. However, two of these patients (cases 8 and 9) temporarily excreted normal amounts of urinary calcium and even values as low as 20 mg. per day, indicating periods of bone repair.

Analysis of the data indicates that the kidneys are able to clear considerable amounts of calcium and thus prevent the occurrence of hypercalcemia. The highest urinary calcium excretion occurring with normal serum calcium levels was 0.643 gm. per day. When the serum calcium levels were normal, the urinary calcium excretion averaged 217 ± 34 mg. per day. When the serum calcium was elevated above 12 mg. per 100 cc., the calcinuria averaged 614 ± 29 mg. per day. The differ-

vascular Research Group. These studies are now in progress and will be reported in a future paper. The data at hand indicate that hypercalcemia resulting from osteolytic metastases is not caused by a primary renal impairment, but that the renal dysfunction is secondary to prolonged hypercalcinuria and hypercalcemia. In the earliest stages of hypercalcemia, normal glomerular and tubular function has been observed. However, maintained hypercalcemia and hypercalcinuria soon result in renal impairment. It is noteworthy that, in spite of renal impairment secondary to hypercalcemia, the kidneys continue to excrete large amounts of calcium and phosphorus as long as the osteolysis continues.

The sequence of events of hypercalcemia secondary to osteolytic metastases appears to be: (1) excessive bone breakdown, (2) mobilization of calcium and phosphorus, (3) hypercalcinuria and hyperphosphaturia, (4) hypercalcemia, and (5) renal impairment.

The process may be reversible if the primary condition of bone catabolism is brought under control.

EFFECT OF INCREASED CALCIUM INTAKE ON METABOLISM OF OSTEOLYTIC METASTASES

The data already presented indicate that in osteolytic metastases there is a loss of minerals which are excreted mainly through the kidneys. It has also been noted that, in osteolysis, the fecal excretion of calcium exceeds the intake, indicating an excretion through the bowel of endogenous calcium from bone catabolism. Metabolic methods alone cannot determine

TABLE 3.—Average Metabolic Data of Five Patients with Breast Carcinoma on a Low Calcium Diet Supplemented with Calcium Gluconate

Intake *	Case No.	Periods	Nitrogen, Mg./Day, Balance	Calcium, Mg./Day			Phosphorus, Mg./Day			
				Urine	Stool	Balance	Urine	Stool	Balance	Un-accounted for
Low calcium.....	1, 3, 5, 6, 8	14	+1,306	194	195	-247	314	182	+57	+83
High calcium.....	1, 3, 5, 6, 8	10	+ 417	211	457	- 81	292	275	-55	-46

* Intake of calcium from the low calcium diet was approximately 150 mg. per day. Supplementation of calcium gluconate given orally raised the total calcium intake to approximately 600 mg. per day.

ence of these means is statistically significant. In every instance of hypercalcemia, the urinary calcium excretion was higher than 0.35 gm. per day. Thus, although hypercalcinuria was consistent with normal serum calcium values in some instances, hypercalcemia was always accompanied by hypercalcinuria.

Consistent correlation was not noted between serum phosphorus level and urinary phosphorus excretion. Likewise, consistent correlation was not noted between serum phosphorus and serum calcium values.

MECHANISM OF HYPERCALCEMIA SECONDARY TO OSTEOLYTIC METASTASES AND ITS EFFECT ON RENAL FUNCTION

In a previous report,¹³ the incidence of spontaneously occurring hypercalcemia in patients with osteolytic breast carcinoma was reported to be 14%. In another report,¹⁴ hypercalcemia induced by hormonal therapy in several types of malignancy was described. The importance of early recognition and prompt therapy of the hypercalcemic crisis with its attendant syndrome of nausea, pernicious vomiting, lethargy, coma, oliguria, and anuria has been stressed. The association of hypercalcemia and renal damage has been noted, but their relationship has not been defined.

Hypercalcemia in patients with osteolysis has been observed during metabolic studies (fig. 2).¹² Renal clearance studies are being performed in collaboration with Dr. Louis Leiter's Cardio-

how much of the fecal content is composed of unabsorbed dietary calcium and how much represents endogenous excretion. However, some information was obtained on the utilization of exogenous calcium by feeding the patients additional calcium. Calculation of turnover rates of isotopic calcium and phosphorus is planned to elucidate this problem.

It is evident that a low calcium diet containing 0.15 gm. of calcium per day is insufficient to replace the calcium lost by osteolysis. This situation is further aggravated by an "unphysiologic" calcium-phosphorus ratio of 1:4 in the diet, with a relative preponderance of phosphorus. Therefore, after control periods on a low calcium diet, the intake of five patients was supplemented with calcium gluconate to increase the calcium intake to approximately 0.6 gm. per day, bringing the calcium-phosphorus ratio to 1:1. The results are summarized in table 3.

Increasing the calcium intake did not change the urinary calcium excretion significantly. The fecal calcium increased under the higher intake, but to less than the increment in intake, resulting in an improvement of the calcium balance. Analysis of the data indicates that the calcium balance was improved by 0.166 gm. per day. This represents 38% utilization of the calcium added to the intake. This percentage of utilization is similar to that reported in normal persons for calcium gluconate, calcium citrate, and the calcium in milk.¹⁵ Therefore, the absorption of calcium through the intestinal tract appears to be unimpaired in these patients.

During calcium gluconate supplementation, the urinary phosphorus decreased slightly and the fecal excretion increased significantly, resulting in a reversal from positive phosphorus balance to a negative one. The unutilized calcium apparently combines with phosphorus and is possibly excreted as some calcium phosphate salt, explaining the increase in fecal phosphorus. This assumption is supported by data derived from table

13. Swyer, A. J.; Berger, J. S.; Gordon, H. M., and Laszlo, D.: Hypercalcemia in Osteolytic Metastatic Cancer of the Breast, *Am. J. Med.* 8: 72 (June) 1950.
14. Hermann, J. B.; Krsten, E., and Krakauer, J. S.: Hypercalcemic Syndrome Associated with Androgenic and Estrogenic Therapy, *J. Clin. Endocrinol.* 9: 1 (Jan.) 1949.
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3. Of the 0.443 gm. of calcium added to the intake, 0.277 gm. apparently remained unabsorbed and was excreted in the feces. This amount of calcium would require 0.143 gm. of phosphorus to form $\text{Ca}_3(\text{PO}_4)_2$; the change in unaccounted phosphorus was 0.129 gm.

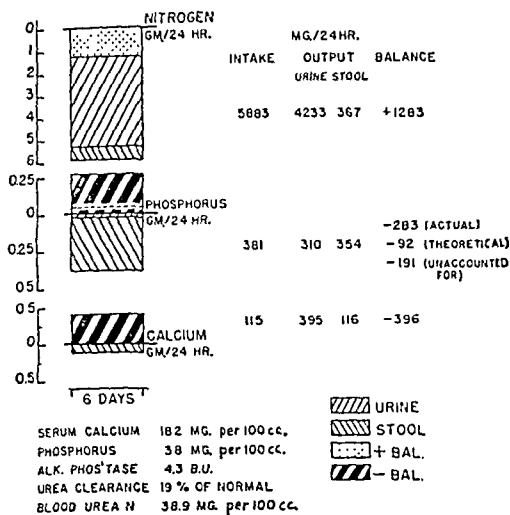


Fig. 2.—Metabolic data of a patient with advanced breast carcinoma, osteolytic metastases, and hypercalcemia (case 2). The metabolic graph is charted according to Reifstein, Albright, and Wells.¹¹ The heavy horizontal line at zero in the nitrogen, phosphorus, and calcium balance graphs indicates the equilibrium between intake and output. Intake is charted from the zero line downward. Output is charted from the intake line upward toward the zero line. The lower hatched area represents fecal excretion, and the hatched area above, urinary excretion. The heavily shaded area above the zero line indicates negative balance; the dotted area below zero indicates positive balance. One unit of the phosphorus scale equals 15 units of the nitrogen scale and 2 units of the calcium scale.

SIGNIFICANCE OF THEORETICAL AND UNACCOUNTED PHOSPHORUS BALANCES

Phosphorus balance depends upon the metabolism of two body constituents, tissue protein and bone. Tissue protein contains phosphorus and nitrogen in the average ratio of approximately 1:15. Bone contains phosphorus and calcium in the average ratio of approximately 1:2.2. Therefore, by using these ratios, a theoretical phosphorus balance can be calculated from the calcium and nitrogen balances. The theoretical phosphorus balance should agree, within the 10% range of experimental error, with the phosphorus balance determined analytically. Any discrepancy between these values is expressed as the unaccounted phosphorus. This method has been advocated by Reifstein, Albright and Wells¹¹ as a means of checking the accuracy of the metabolic data and "to emphasize any situation where the measured balances differ from the theoretical balances."

In the series here reported, significant changes in the unaccounted phosphorus were achieved by changing the calcium intake (table 3). On a low calcium diet that contains the "unphysiologic" calcium-phosphorus ratio of 1:4, there is an unaccounted phosphorus retention. By supplementing calcium gluconate to the intake, the diet contains a calcium-phosphorus ratio of 1:1, and the unaccounted phosphorus is close to zero. This applies to patients with normal calcinuria and normal calcium balance. If, however, there is extensive bone catabolism, the excess endogenous calcium appears to combine with phosphorus. Even on a low calcium diet, the unaccounted phosphorus approximates zero, while calcium gluconate supplementation results in an unaccounted phosphorus loss.

Pearson and co-workers¹⁶ found in lymphoma patients an unaccounted phosphorus loss occurring during ACTH therapy which they could interpret as indicative of tumor breakdown (i. e., protoplasm that is rich in phosphorus content). However, data from the present study indicate that the unaccounted phosphorus is influenced by the ratio of calcium to phosphorus available for metabolism. If a simple measure such as varying the calcium intake can cause major changes in the unaccounted

phosphorus, it appears unlikely that the unaccounted phosphorus in all instances can be used as a reliable index of tumor growth or recession.

METABOLIC AND CLINICAL MANIFESTATIONS OF OSTEOLYTIC METASTASES SECONDARY TO BREAST CARCINOMA COMPARED TO THOSE OF OTHER PRIMARY NEOPLASMS

Osteolytic metastases occur secondary to many types of neoplasia. The clinical manifestations of osteolytic metastases are similar in all: bone pain, secondary anemia, tendency to fracture, and the possibility of hypercalcemic crisis. The metabolic behavior of other osteolytic tumors has been investigated to determine whether it is similar in various tumors. For comparison, metabolic studies have been performed in patients with osteolysis secondary to thyroid carcinoma, leiomyosarcoma,¹² and multiple myeloma. In all instances, the metabolic pattern was similar to that already described for osteolytic metastases secondary to breast carcinoma. Hypercalcinuria, hyperphosphaturia, negative calcium and phosphorus balances, and, in some instances, hypercalcemia, also were observed in these cases. Figure 4 illustrates this point.

This patient had multiple myeloma, extensive osteolysis, and hyperglobulinemia. His metabolism was studied for 36 days. In the first 12 days, the serum calcium and blood urea nitrogen were normal, and the mineral metabolism was typical for osteolysis. During the following 18 days, there was a spontaneous acceleration of osteolysis with increasing hypercalcinuria, hyperphosphaturia, and negativity of the calcium and phosphorus balances. This resulted in hypercalcemia. It is interesting to note

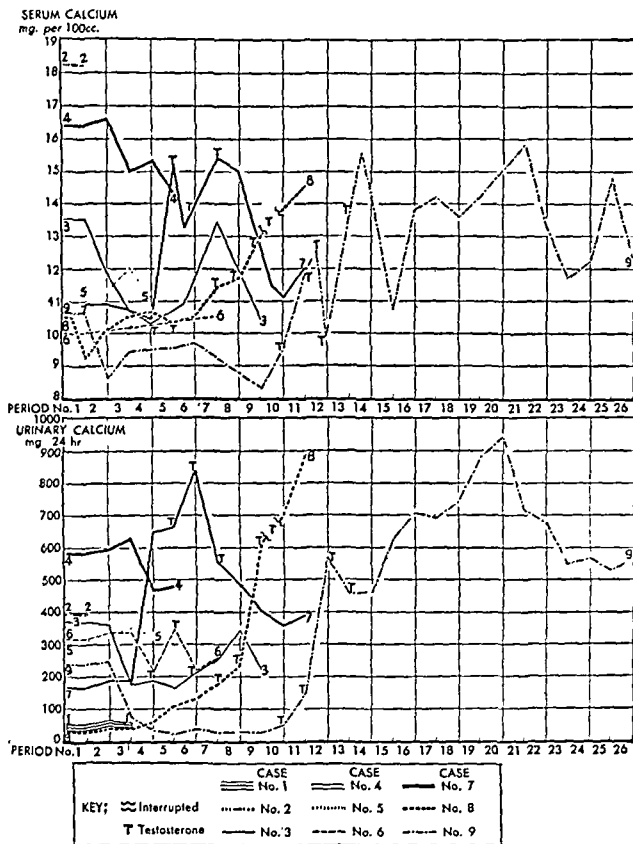


Fig. 3.—Relationship of serum calcium to urinary calcium. In the upper graph is plotted the serum calcium, and in the lower, the urinary calcium of the nine patients with breast carcinoma.

that the serum protein remained approximately at the same level, so the hypercalcemia cannot be attributed to a change in serum protein. In the last six days of study, calcium and

16. Pearson, O. H.; Eliel, L. P.; Rawson, R. W.; Dobriner, K., and Rhoads, C. P.: ACTH—and Cortisone—Induced Regression of Lymphoid Tumors in Man, *Cancer* 2: 943 (Nov.) 1949.

phosphorus metabolism improved spontaneously, resulting in a return of the serum calcium and urea nitrogen to normal.

These control studies in osteolysis secondary to other tumors indicate that the metabolic changes are not specific for breast carcinoma, but are characteristic of a destructive bone process.

METABOLIC AND CLINICAL MANIFESTATIONS OF OSTEO-
LYTIC METASTASES COMPARED TO THOSE OF
OSTEOBLASTIC METASTASES

It has been found that osseous metastases from breast, thyroid, renal, and pulmonary carcinoma are predominantly osteolytic, whereas the osseous metastases from prostatic carcinoma are predominantly osteoblastic; careful microscopic examination of metastatic bone lesions reveals areas of both mineral breakdown and overgrowth with one or the other predominating. Since the nineteenth century, many investigators have sought to discover why one type of metastatic tumor causes bone breakdown whereas another incites the opposite effect. The theories have been reviewed by Ashburn,¹⁷ but none has been established.

Clinically, the two types of bone response result in some manifestations that are similar and others that differ. Pain and anemia are frequent manifestations of both. However, fractures and hypercalcemia are complications of osteolytic metastases that rarely occur in osteoblastic cases.

Metabolically, the two types show characteristic differences. Aub and co-workers studied seven cases of prostatic carcinoma with osteoblastic metastases⁹; the authors' group has studied seven cases of prostatic carcinoma and a patient with osteoblastic metastases secondary to pulmonary carcinoma. A typical case has been reported^{10d} and the series will be presented in a future report. In contrast to the negative mineral balances characteristic of osteolytic patients, osteoblastic metastases are characterized by an avidity for mineral retention with subnormal urinary calcium excretion and abnormal calcium retention (fig. 5).

sarily a steadily progressive disease, but may proceed in waves of exacerbations and remissions.

3. The mineral loss caused by osteolytic breast cancer metastases is characterized metabolically by high urinary excretion of calcium and phosphorus with negative mineral balances. The protein balance is not specific, and even advanced cases may be maintained in a state of nitrogen equilibrium.

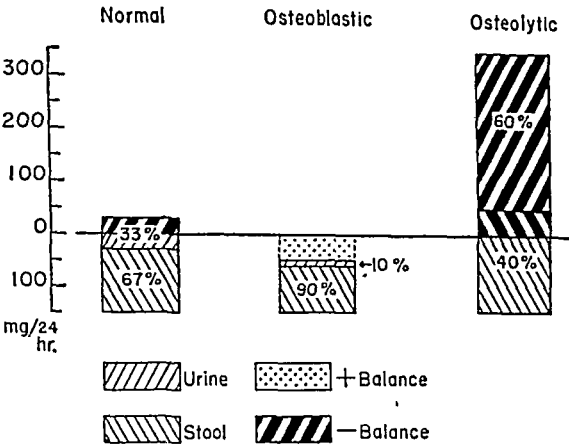


Fig. 5.—Schematic representation of calcium balance in normal persons and in patients with osteoblastic and osteolytic metastases.

4. A similar mineral loss is seen in patients with osteolytic metastases secondary to other malignancies. Therefore, this metabolic process is not specific for breast carcinoma but is characteristic of skeletal destruction.

5. The excessive and prolonged mineral loss in patients with osteolytic metastases may result in hypercalcemia. The sequence of events in such instances appears to be: excessive bone breakdown, mobilization of calcium and phosphorus, hypercalcinuria and hyperphosphaturia, hypercalcemia, and finally renal impairment.

6. In contrast to the mineral loss caused by osteolytic metastases is the calcium retention caused by osteoblastic metastases. The metabolism of patients with osteoblastic metastases is characterized by subnormal urinary calcium excretion.

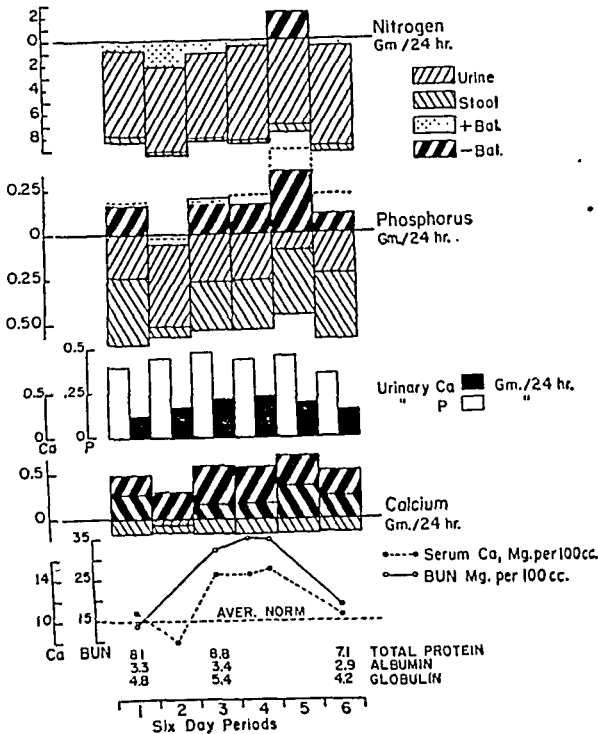


Fig. 4.—Metabolic data of a patient with multiple myeloma, illustrating spontaneous hypercalcemia in periods 3, 4, and 5.

SUMMARY

1. Correlation of clinical and metabolic data of patients with metastatic malignancy leads to a better understanding of the natural course and mechanism of the disease process and forms a baseline upon which therapeutic measures can be more accurately evaluated.
2. Metabolic evidence as well as clinical observation indicates that even advanced metastatic malignancy is not neces-

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, M.D., Secretary.

Dihydroxy Aluminum Aminoacetate (See New and Nonofficial Remedies 1951, p. 311).

Smith-Dorsey, Division of the Wander Company, Lincoln, Neb.

Gel Doraxamin: 473 cc. bottles. A gel containing 0.1 gm. of dihydroxy aluminum aminoacetate in each cubic centimeter. Preserved with 0.015% of butyl *p*-hydroxybenzoate.

Tablets Doraxamin: 0.5 gm.

Dimethyl-Tubocurarine Iodide (See New and Nonofficial Remedies 1951, p. 162).

Chemo Puro Manufacturing Corp., Long Island City, N. Y.

Powder Dimethyl-Tubocurarine Iodide: Bulk; for manufacturing use.

Estrone-U.S.P. (See New and Nonofficial Remedies 1951, p. 333).

Meyer Chemical Company, Inc., Detroit.

Solution Estrone in Oil: 10 cc. vials. A solution in sesame oil containing 1 mg. of estrone in each cubic centimeter. Preserved with 0.5% chlorobutanol.

Mephenesin (See New and Nonofficial Remedies 1951, p. 165).

Organon, Inc., Orange, N. J.

Tablets Oranixon: 0.5 gm. U. S. Trademark 532,165.

17. Ashburn, L. L.: New Bone Formation in a Primary Carcinoma of the Prostate Gland, Arch. Path., 28: 145 (Aug.) 1939.

COUNCIL ON FOODS AND NUTRITION

ACCEPTED FOODS

The following products have been accepted as conforming to the rules of the Council on Foods and Nutrition.

JAMES R. WILSON, M.D., Secretary.

Haas, Baruch and Company, Los Angeles, Calif.

HAAS BRAND DIETETIC PACK TUNA CHUNKLETS. Ingredients: Light meat tuna and distilled water.

Analysis (submitted by distributor).—Total solids 30.6%, moisture 69.4%, protein (N $\times$ 6.25) 28.3%, fat 0.75%, carbohydrates (by difference) 0.15%, sodium 40 mg./100 gm.

Calories.—1.22 per gram; 34.6 per ounce.

Use.—A useful adjunct for the planning of low fat, low sodium diets.

Mead Johnson & Company, Evansville, Indiana.

PROBANA. Ingredients: A blend of Mead's Powdered Protein Milk, Protolysate (a dried enzymic digest of casein), banana powder, and dextrose.

Analysis (submitted by manufacturer).—Total solids 98%, moisture 2%, ash 4%, fat 14%, protein (N $\times$ 6.25) 27%, carbohydrate (by difference) 51%, and lactic acid 2%.

Minerals	Mg. per 100 Gm.
Calcium	800
Phosphorus	600
Iron	2

Calories.—4.4 per gram; 125 per ounce.

Use.—Probana may be used in the nutritional support of infants with cystic fibrosis of the pancreas, steatorrhea due to various causes including severe celiac disease, and chronic and acute diarrhea during infancy.

The Council on Foods and Nutrition has authorized the publication of this report on the sodium content of commercial spices because of the wide current interest in low-sodium diets and the use of spices in such diets.

JAMES R. WILSON, M.D., Secretary.

SODIUM CONTENT OF COMMERCIAL SPICES

C. A. Elvehjem, Ph.D.

and

C. H. Burns, M.S., Madison, Wis.

Diets restricted in sodium are now accepted therapy in a number of pathological conditions; for example, a reduction of the mineral sodium in addition to excessive calories is one of the principal focuses of present-day therapy of high blood pressure. One of the limitations in the production of low-sodium diets is a lack of knowledge of this element in various dietary constituents. Since the addition of spices is often recommended in diets low in salt in order to improve acceptability, the sodium content of these spices is of importance. The following study was undertaken to secure this information.

Samples of spices were made available by several of the manufacturers through the American Spice Trade Association, Inc. In each case, regular commercial packages were submitted. A total of 132 samples was received, of which 100 were analyzed for sodium. The samples were prepared according to a method similar to that described by Meyer and co-workers,¹ and a Perkins-Elmer Model 52A Flame Photometer was used for the analysis. One-gram samples were weighed into covered beakers and treated with about 50 ml. of concentrated nitric acid. After partial digestion, the mixture was heated at medium heat until the solution was pale yellow and clear. The solution was then allowed to go to dryness on low heat and charring was avoided. More consistent results are obtained if samples are not ashed to whiteness by prolonged treatment. The ash was then taken up in 25 ml. of 1% nitric acid containing 400 ppm of lithium,

which serves as an internal standard for the flame photometer. The solution was filtered through Whatman no. 42 filter paper, and the filtrates were read directly on the instrument.

Each sample was analyzed in duplicate and a few in triplicate. At least two samples of each spice obtained from different sources were analyzed. Remarkably good correlation was obtained between spices obtained from different companies. The only variation observed was a higher content of sodium in cer-

Sodium Content of Commercial Spices

Spice	Sodium, %
Allspice—ground	0.12
Anise—seed	0.013
Basil (Laurel)—leaves	0.016
Bay—leaves	0.027
Caraway—seed	0.027
Cardamom—seed	0.022
Cardamom—ground, decorticated	0.011
Cassia—cracked	0.016
Cassia—buds	0.012
Celery—seed	0.14
Celery—flakes, dehydrated	2.3
Cinnamon—ground	0.021
Cloves—ground	0.021
Cloves—whole	0.023
Coriander—seed	0.040
Cumin—ground	0.014
Curry—powder	0.004
Dill—seed	0.018
Fennel—seed	0.052
Fonugreek—seed	0.086
Fonugreek—ground	0.089
Garlic—powder	0.022
Ginger—whole	0.016
Ginger—ground	0.042
Mace—whole	0.15
Mace—ground	0.082
Marjoram—powdered	0.032
Marjoram—leaf	0.049
Marjoram—rubbed	0.083
Mint—flakes, dehydrated	0.043
Mustard—ground	0.010
Mustard—seed	0.009
Nutmeg—whole	0.011
Nutmeg—ground	0.024
Onion—powder	0.093
Oregano—leaf	0.031
Paprika—ground	0.071
Parsley—flakes, dehydrated	0.49
Pepper—black, ground	0.019
Pepper—black, whole	0.014
Pepper—red, ground	0.028
Pepper—red, whole	0.014
Pepper—white, ground	0.009
Pepper—white, whole	0.007
Poppy—seed	0.011
Rosemary—leaves	0.048
Saffron—Spanish	0.024
Sage—rubbed	0.014
Savory—powdered	0.017
Savory—rubbed	0.054
Sesame—seed	0.060
Thyme—powdered	0.043
Thyme—leaf	0.017
Thyme—ground	0.024
Thyme—rubbed	0.040
Turmeric—ground	0.066
Turmeric—whole	0.015
Vanilla—beans	0.018

tain samples of ground spice than in the original spice. At present we have no explanation for this variation, but, since all samples were so low, the variation is insignificant.

The average values are given in the table. Many of the figures range from 0.01 to 0.02% sodium. Most of the values are below 0.05%, and all are below 0.1%, with the exception of allspice, celery seed, dehydrated celery flakes, whole mace, and dehydrated parsley flakes. These figures indicate that, with the exception of celery flakes and parsley flakes, the amount of sodium contributed through the usual amount of spices used is insignificant, and that most spices can be used safely in low-sodium diets.

From the department of Biochemistry, University of Wisconsin.
1. Meyer, J. H., and others: Sodium, Potassium, and Chlorine Content of Feeding Stuffs, J. Animal Sc. 9: 153, 1950.

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NEW ANTITUBERCULOSIS DRUGS

The popular press has recently given widespread publicity to a series of new antituberculosis drugs, the hydrazine derivatives of isonicotinic acid. Headlines have proclaimed them "wonder drugs" and have suggested that they may eradicate tuberculosis within a few years. It is regrettable that such glowing announcements have been made to the public before clinical evaluation of the drugs is complete and before they are available to other than a few investigators. As has happened before in connection with other new therapeutic agents, the hopes of many patients have been raised prematurely and perhaps unjustifiably. These drugs have shown remarkable activity against the tubercle bacillus in the test tube, in the experimental animal, and in preliminary tests in man, but no final statement can yet be made as to the optimum dosage schedule, the permanency of the early results obtained, or the possibility of the development of drug resistance. Until their proper role in the treatment of tuberculosis has been determined, these compounds should be used only under strictly controlled experimental conditions. Physicians should inform their patients that the new drugs are not available in interstate commerce and that more studies are needed before they can be made available.

The chemotherapeutic activity of the compounds under investigation was discovered independently by the research staffs of Hoffmann-LaRoche, Inc., and E. R.

1. (a) Grunberg, E., and Schnitzer, R. J.: Studies on the Activity of Hydrazine Derivatives of Isonicotinic Acid in the Experimental Tuberculosis of Mice, *Quart. Bull., Sea View Hosp.* 13:3 (Jan.) 1952. (b) Bernstein, J.; Lott, W. A.; Steinberg, B. A., and Yale, H. L.: Chemotherapy of Experimental Tuberculosis: V. Isonicotinic Acid Hydrazide (Nydrazid) and Related Compounds, *Am. Rev. Tuberc.*, to be published.

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7. Elmendorf, D. F., Jr.; Cawthon, W. V.; Muschenheim, C., and McDermott, W.: The Absorption, Distribution, Excretion and Short Term Toxicity of Isonicotinic Acid Hydrazide (Nydrazid) in Man, *Am. Rev. Tuberc.*, to be published.

Squibb & Sons in the course of a systematic screening of the thiosemicarbazones and related substances for antituberculosis activity. The most active compound in the group, isonicotinic acid hydrazide, was synthesized by both of these groups and has been given the trade name of rimifon® by Hoffmann-LaRoche and nydrazid® by Squibb. In the test tube this compound is bacteriostatic for *Mycobacterium tuberculosis* in low concentrations (0.02 to 0.05 µg per milliliter).¹ In the experimentally infected animal it appears to have two advantages over agents previously used. It is quantitatively more effective than streptomycin, *p*-aminosalicylic acid, niacinamide, or any of the thiosemicarbazones tested,² and it differs qualitatively from these agents in that it appears to be bactericidal rather than bacteriostatic. Following treatment of animals with any of the preparations just mentioned, viable tubercle bacilli can be recovered on culture even in the absence of gross lesions. Following treatment with isonicotinic acid hydrazide or its isopropyl derivative (1-isonicotinyl-2-isopropylhydrazine), no bacilli can be found in the majority of animals^{1a} and pulmonary lesions do not appear within 21 days after cessation of therapy, as they do in animals treated with streptomycin, *p*-aminosalicylic acid, or any of the other tuberculostatic drugs.^{2b} In vitro evidence of bactericidal activity has also been obtained.³ The protective and therapeutic value of the hydrazides of isonicotinic acid has been demonstrated in a variety of species, including the mouse,^{1a} guinea pig and rabbit,³ and monkey.⁴

Trials of the new drugs in man are now in progress in a number of institutions. At Sea View Hospital on Staten Island, 92 patients with moderately or far advanced pulmonary tuberculosis not responding to streptomycin, *p*-aminosalicylic acid, or other measures have been treated with isonicotinic acid hydrazide or its isopropyl derivative for 4 to 15 weeks.⁵ Daily oral doses of 2 to 4 mg. per kilogram of body weight of the former drug and 2 to 10 mg. per kilogram of body weight of the latter drug have been used. Within two to three weeks, fever and malaise disappeared in every case, cough and expectoration were completely or almost completely eliminated, and remarkable increases in appetite and weight occurred. Bacilli disappeared from the sputum in 25% of the patients in 4 to 15 weeks, and sharp decreases in the number of bacilli occurred in another 29%. Reduction in cavity size was noted in 23 cases, but cavity closure occurred in only 2 cases. Exudate disappeared in 17 patients and increased in 4. One questionable new cavity appeared at the site of a previous exudate. Cure or pronounced improvement was seen in cases of tuberculous laryngitis, otitis, and glossitis. Important chemotherapeutic effects were also seen in tuberculous meningitis and gastroenteritis, and in tuberculous diseases of bone and joint.⁶ In preliminary studies at New York Hospital-Cornell Medical Center,⁷ another series of patients has been treated with 3 mg. of isonicotinic acid hydrazide per kilogram of body weight daily for 4 to 16 weeks, but the Cornell investigators believe it is too early to make any positive statement about the value of this compound in the treatment of tuberculosis. Substantial gains in appetite and body weight and reduction in fever were observed in some but

not all of the patients. Many of these patients had been subjected to the appetite reducing effects of *p*-aminosalicylic acid immediately before this study.

Evidence of drug toxicity was not seen in the Cornell study, but at Sea View Hospital a variety of toxic manifestations were encountered.⁸ These included symptoms suggesting central nervous system stimulation (hyperactive deep reflexes, leg twitching, and insomnia), symptoms suggesting modification of autonomic activity (dryness of the mouth, bladder sphincter disturbances, and constipation), and dizziness presumably due to transitory moderate decreases in blood pressure. Although patients taking the drug showed occasional albuminuria and cylindruria and a transitory drop in hemoglobin values, averaging 0.5 gm., during the fourth and fifth weeks, there was no clinical or autopsy evidence of serious damage to kidneys, bone marrow, or liver. Kidney and liver damage have been observed in the monkey,⁴ dog⁹ and rat,¹⁰ following the administration of moderate or large doses for several weeks, and hemopoietic disturbances have occurred in some of these species. There is a wide margin of safety between the therapeutic and lethal dose in animals, about 20 times the oral therapeutic dose being necessary to kill 50% of mice.¹¹ Death is preceded by convulsions and respiratory arrest.

The route of administration of these drugs seems to make little difference in the dose required. Following oral administration of isonicotinic acid hydrazide in man, the compound is rapidly absorbed and a high percentage is excreted in the urine during the first 24 hours.⁷ After a single oral dose of 3 mg. per kilogram of body weight, the maximum concentration in the plasma (1.3 to 3.4 μ g per milliliter) is attained in one to six hours after administration. Appreciable concentrations of the drug are present in the spinal fluid within three hours after an oral dose of 2 to 3 mg. per kilogram in patients without meningitis. In patients with tuberculous meningitis the concentrations in the spinal fluid are substantially higher than the concentrations necessary to inhibit *M. tuberculosis* in vitro.

Attempts to obtain drug resistant organisms by culturing strains of *M. tuberculosis* in increasing concentrations of isonicotinic acid hydrazide have not been successful³ and no clinical evidence of bacterial resistance has been encountered.¹² Sufficient time has not yet elapsed, however, to conclude that drug resistance will not eventually develop.

The chemotherapeutic specificity of these compounds for the tubercle bacillus is indicated by the fact that none of them has shown any activity in vivo against *Streptococcus hemolyticus*, *Pneumococcus pneumoniae* type 1, *Salmonella schottmuelleri*, *Trypanosoma equiperdum*, *Trichomonas vaginalis*, or the influenza virus of mice.¹³

It is evident that this group of compounds has several advantages over other antituberculosis agents. Whether they will provide definitive treatment or whether they will prove to be merely helpful adjuvants can be determined only by prolonged investigation. Until their potential dangers are thoroughly studied and their proper place in the total scheme of treatment is determined, they should not be used indiscriminately.

THE EASTER SEAL APPEAL

According to many philanthropic organizations, it is a tradition of American medicine that where there is a need, physicians will find a way to meet the need. Perhaps this is why the Easter Seal appeal is of special interest to the medical profession. Through Easter Seal facilities and services literally hundreds of physicians are helping to find a way for crippled children to have healthier, happier, and more useful lives.

Nationwide programs for crippled children have been planned by the National Society for Crippled Children and Adults, in close cooperation with and under the direction of liaison officers appointed by the American Medical Association, medical specialty groups, and other allied professional organizations. Similarly, at the state and local levels, physicians have an important place on advisory committees and councils. But this is not the only interest of physicians in this work. Through the more than 500 specific facilities maintained by the Easter Seal societies and through the specialized skills of their more than 2,000 therapists, psychologists, medical social workers, and others of the ancillary professions, doctors are able to augment their own diagnosis and treatment of crippled children.

Still another aspect that is significant to American physicians is that the Easter Seal societies are a purely voluntary way of providing help for those unable to obtain it for themselves—a dramatic demonstration of the sense of personal responsibility for the welfare of one's neighbor. Last year this help was extended to nearly a quarter of a million crippled children and adults.

Because this is a voluntary effort, its major source of support is the American people themselves—millions of individual donors who are asked only through the annual Easter Seal appeal to give their dollars. This year the appeal began March 13 and will continue through Easter Sunday, April 13. During that time, the National Society and its affiliates hope to raise funds to support a 10 million dollar program. In a period of rising costs, they explain, services for crippled children, always expensive, will cost more than ever before. If less than 10 million dollars is received, a curtailment of services will be necessary, and it will be impossible to help children who have come recently to the Easter Seal societies needing treatment and training.

The support of the medical profession of this nation is vital to this cause. By sharing the leadership in seeing that the Easter Seal appeal is successful, physicians can once more demonstrate to their fellow Americans that where there is a demonstrated need, physicians will help find a way to meet the need.

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9. Rubin, B.; Hassert, G. L., Jr.; Thomas, B. G. H., and Burke, J. C.: Pharmacology of Isonicotinic Acid Hydrazide (Nydrazid), *Am. Rev. Tuberc.*, to be published.

10. Benson, W. M.; Stepko, P. L., and Roe, M. D.: Pharmacologic and Toxicologic Observations on Hydrazine Derivatives of Isonicotinic Acid (Rimifon, Marsilid), *Am. Rev. Tuberc.*, to be published.

11. Rubin, B.; Hassert, G. L., Jr.; Thomas, B. G. H.; Grunberg and Schnitzer.¹²

12. Robitzek, Selikoff, and Ornstein.¹⁴ Elmendorf, Cawthon, Muschenheim and McDermott.⁷

THE PRESIDENT'S PAGE

A SPECIAL MESSAGE

A short time ago I received a letter from a prominent labor leader, one who is a friend of medicine. He told the following story: "Recently, in a western city, a surgeon performed an operation for uncomplicated appendicitis upon a woman patient. The operation and convalescence were routine. The fee was \$150. In the same week the same surgeon performed the same operation upon another woman. It was also routine and also without complications. The fee was \$300."

The labor leader went on to say that the only difference between the two cases was that the first woman had no sickness insurance, while the second woman was insured under a union health plan. He charged that the surgeon had doubled the second woman's bill deliberately. What, he wanted to know, was the medical profession doing about such unfair practices?

This instance has not been investigated, and we therefore lack complete knowledge concerning it. This complaint, however, can be matched with similar stories from private insurance companies, Blue Shield plans, and individuals. How frequent are complaints of this nature? I do not know, because the American Medical Association does not hear about all such cases, but the complaints are frequent enough to warrant serious action by medical associations to correct these abuses.

In order to determine how widespread this practice of increasing fees may be, appropriate agencies of the American Medical Association are undertaking a comprehensive study. These agencies will request documented case histories from several large unions, from farm groups, from private insurance companies, and from nonprofit insurance groups. Instances occurring between Jan. 1 and April 1, 1952, will be investigated. When this study has been completed, medical societies will know the extent of such practices and will have facts upon which to base programs for control of this abuse. Needless to say, however, they should not wait for publication of the report before stating their strong opposition to such conduct.

It is difficult for me to believe that intentional raising of fees for persons carrying sickness insurance is widespread in the profession. Undoubtedly a small number of physicians are guilty of this practice, but their activities are bringing discredit to us all. Such physicians who are members of our medical societies must be held strictly to account and promptly disciplined when the occasion warrants.

I would remind all physicians, and especially those who serve on medical society grievance committees, of the sentence in our Principles of Medical Ethics that reads, "A physician should expose, without fear or favor, incompetent or corrupt, dishonest or unethical conduct on the part of members of the profession." Neglect of this key sentence leads to the harboring of unethical physicians within our ranks. If we tolerate them, we have no

one but ourselves to blame when the public brings damaging charges against us.

While some of the complaints of increased fees for insured patients are justified, I am certain that many others, perhaps most, arise out of misunderstanding. Sometimes, in their zealous effort to sell insurance, salesmen lead the subscriber to believe that his hospital and surgical bills will be covered entirely by his policy, when this may not be the case. Under these circumstances, when the physician's bill or the hospital bill exceeds the limit of payment allowed by the policy, the patient blames the doctor or the hospital.

Misunderstanding of this type can be forestalled in two ways. One is for medical societies to appeal to insurance carriers and their representatives in their localities to make and keep their

literature and sales talks factual. This applies both to commercial and Blue Cross-Blue Shield plans. Patients should be informed that much insurance is not designed to cover all medical costs but is intended to take the economic shock out of illness by protecting them against some of the insurable costs of health care.

Another way to forestall misunderstanding is for individual physicians to take time to discuss finances with their patients. Tell your patient what your standard fee is. Your patient then will be able to discuss his coverage with his insurance adviser and will understand beforehand the extent to which his medical costs will be met by his insurance. Another advantage of such discussion is that you will ascertain the financial status of your patient. When he is in a low-income group or has heavy obli-

gations you can adjust your fee accordingly. Perhaps you will wish to arrange time payments to ease his burden. I know that most physicians desire to make their services available on a fair basis and one that will be most helpful to the patient. Failure to ascertain essential facts produces unintentional imposition on some patients.

Voluntary insurance against sickness has been sold to the American people as a practical means of protecting themselves from unexpected and perhaps overwhelming medical costs. The value of these plans must not be destroyed by the few physicians who view them as an opportunity to collect an increased fee. Voluntary prepayment plans are the medical profession's greatest bulwark against the socialization of medicine. This program must not be jeopardized by avaricious physicians who have not learned that liberty depends upon individual integrity and responsibility. Unfair and unethical conduct by a small, irresponsible segment of the profession not only harms the patients involved but endangers the freedom of medicine. These practices must be eliminated!

JOHN W. CLINE, M.D., San Francisco.



ORGANIZATION SECTION

STATEMENTS BY A. M. A. REPRESENTATIVES ON PROPOSED EMERGENCY MATERNAL AND INFANT CARE PROGRAM BEFORE SENATE COMMITTEE

Mr. Chairman and members of the Committee: My name is Edwin S. Hamilton. I am engaged in the active practice of medicine in Kankakee, Ill., and am a member of the Board of Trustees of the American Medical Association. I am appearing here today with my colleague, Dr. Woodruff L. Crawford, on behalf of that Association in opposition to S. 1245 and S. 2337, which are under consideration by your committee. Although the two bills are dissimilar in many details, I believe it will be sufficient for the purposes of my statement to note that both measures propose the reestablishment of an emergency maternity and infant care program for the wives and children of enlisted personnel of the armed forces. In addition, S. 2337 would provide a program of hospital care for all dependents of enlisted personnel.

It is believed that this brief reference to the purpose of the bills is sufficient, inasmuch as the basic position of the American Medical Association is that there is no demonstrated need for the activation of a national program of the type proposed. The position of the Association is based on consultations with other interested public and private groups and on comprehensive surveys conducted or sponsored by its Committee on Maternal and Child Care, under the chairmanship of Dr. Crawford. Before asking Dr. Crawford to discuss the details of these conferences and these surveys and their results, I would like to review the more general aspects of the question and outline briefly the history of the activities and interest of the Association in this regard.

Although the legislative proposals under consideration would authorize maternity and infant care for dependents of all enlisted personnel in the armed forces, it is believed that, in determining the need for federal assistance, enlisted men in the first three grades, or those with the lowest income, would be the group first affected. Figures recently released by the Department of Defense show that less than 1 in 10 of the enlisted men in these grades have dependents other than dependent parents and about one-half of that number, or about 1 in 20, have a wife only. Of course, only a part of this number will have children during the two years of an enlisted man's tour of military duty. Of that number, many are already receiving dependent medical care at hospitals of the armed services.

With respect to the remainder, it should be remembered that many servicemen are perfectly able and, in fact, desirous of using the services of their regular physicians without federal financial assistance. I believe that experience shows that only about 50% of the dependents of service personnel who are eligible for medical care make any effort to obtain it.

Then, too, local public and private agencies and organizations that serve the indigent members of the general population are also available to the servicemen who are unable to pay for medical care and hospitalization for their wives and children. The demands on the medical profession for the care of hardship cases are not appreciably greater since the Korean incident. The dedication of a substantial amount of time to the care of persons unable to pay is recognized by the organized profession and the individual physician as a medical responsibility.

The participation and cooperation of the medical profession in the emergency maternity and infant care program that existed

during World War II is well known and therefore would not appear to require any discussion at this time. I should prefer to commence this résumé of the Association's activities about the time of the Mid-Century White House Conference on Children and Youth, which was held in Washington, D. C., in December, 1950. At that meeting the current military status was discussed in relationship to the medical problems of dependents of servicemen and the necessity for reactivating another emergency maternity and infant care program.

This discussion suggested the desirability of obtaining a true picture of the actual need for such a program. A survey of local medical societies and individual physicians was initiated, supplemented by a series of conferences with private and public organizations and national health associations. More recently the first phase of a survey of the situation in the Los Angeles area has been completed.

In summary, let me say that the American Medical Association is opposed to the enactment of S. 1245 and S. 2337 because no evidence has been found that would indicate that the wives and children of enlisted men of the armed forces are not now being cared for by existing facilities and agencies. Further, it is not believed that the need for such a program will be demonstrated in the near future, despite an increase in the total strength of the armed forces. This conclusion is based on the fact that a number of reservists will continue to be released as they complete their tours of duty and that their places will be filled in a large measure through Selective Service processes. The policy of the Selective Service System at this time is not to draft fathers. In actuality, the percentage of enlisted men in the armed forces with dependents has dropped 4.8% during the year 1951. It is the belief of the Association that the activation of a federal Emergency Maternity and Infant Care program at this time with its attendant cost is an unjustified and unnecessary expenditure of federal funds.

If I may, Mr. Chairman, I should like at this time to have Dr. Crawford give to the Committee a more detailed statement as to the surveys and conferences conducted by his Committee and results of these actions.

Statement by Dr. Crawford

My name is Woodruff L. Crawford. I am a physician engaged in the practice of pediatrics in Rockford, Ill., and am Chairman of the Committee on Maternal and Child Care of the Council on Medical Service of the American Medical Association. I would like to enlarge on Dr. Hamilton's remarks relative to the interest and activities of the American Medical Association concerning emergency maternity and infant care.

During the Mid-Century White House Conference on Children and Youth, in December, 1950, it was evident that some thought was being given to the necessity for the reactivation of some plan similar to the Emergency Maternity and Infant Care program of World War II.

With this in mind, the Committee on Maternal and Child Care, in January, 1951, developed a short questionnaire, which it sent to all state medical societies and approximately 400 physicians, representing every state in the union, including general practitioners, obstetricians, and pediatricians. The purpose of the questionnaire was to learn the opinion of the state societies concerning the operation of the Emergency Maternity and Infant Care program during World War II and to get the reactions of physicians who had worked under this program. The survey was

instituted to assist the Committee if and when it was called on to participate in discussions on this subject. The responses received contained a sufficient amount of detailed information to enable the Committee to formulate numerous definite and beneficial suggestions. With the benefit of these findings the Committee members were able to participate actively in a series of meetings from Feb. 13 to April 4, 1951, which were called by officials of the United States Children's Bureau of the Federal Security Agency. These exploratory conferences were attended by staff members from the Children's Bureau, persons representing major health and hospital associations, and others interested in the services that might be provided under an emergency maternity and infant care program. The stated purpose of the conferences was to consider previous experience and obtain suggestions for adapting a maternal and infant care plan to present conditions, should the Congress decide to provide again for such a program.

The results of the conferences were summarized in a series of broad policies on which the participating organizations were able to agree. The policies included such items as the duration of the program, persons to be covered, the scope of services to be provided, the proper agency to administer the program, financing the program, and necessary elements of state plans. It should be noted, however, that all of the conferees, with the exception of the representatives of the Children's Bureau, agreed that the need for such a program had not been demonstrated and that no program should be initiated until the evidence of need became apparent.

In an effort to keep abreast of the situation, the Committee called three subsequent meetings (most recently on Dec. 15, 1951) with representatives of the American Hospital Association, the Catholic Hospital Association, the American Protestant Hospital Association, the American Legion, the Association of State and Territorial Health Officers, the American Academy of Pediatrics, and the American National Red Cross. Although formal actions were not taken at these meetings, it was the consensus of those in attendance that no widespread emergency exists that warrants the inauguration of a federal program for the care of the wives and children of servicemen. Requests for such a program have been infrequent, and when they occur they are usually based on individual instances arising near military installations where the influx of servicemen and their families has resulted in abnormal conditions. When need for assistance has occurred away from military posts, help has been available through local sources.

At one of these meetings, the representative of the American National Red Cross discussed the results of a survey made by that organization in March and April, 1951, at the request of the United States Children's Bureau. The interpretation of these results by the Children's Bureau presented a *prima facie* case of need that was inconsistent with the reports of other associations. Inasmuch as the report of the Red Cross did not indicate the final disposition of any of the cases considered and because of the desire of the Committee to clarify the situation, it was suggested that a follow-up study be made with Red Cross local chapters. Further investigation, however, indicated that the local Red Cross chapters do not keep records of the cases in which they do not give assistance, that many of the requests were based on telephone calls, and that to some extent the data represented estimates. The Committee has also been advised that the Red Cross does not believe such a follow-up study is either feasible or advisable and that it does not want its survey to be interpreted as indicating any national need for an emergency maternity and infant care program.

Despite the fact that the Red Cross has disclaimed any showing of need for an emergency maternity and infant care program by its study, the American Medical Association, after conferring with the various organizations previously referred to, decided

to sponsor an independent and completely scientific survey of this problem. The research department of the welfare council of metropolitan Los Angeles was engaged to inquire into the ability of local servicemen to meet the costs of medical and hospital obstetric care. Los Angeles was selected as representative of one of the more dislocated areas from a military personnel standpoint, with the idea that, if the medical and financial problems are adequately being taken care of there, the same would be true elsewhere in the country. Every serviceman's wife in that area who delivered during the period from Jan. 1 to Jan. 15 was interviewed while in the hospital. Visits were made to each of the 89 hospitals in that district and to servicemen's wives from the Los Angeles area whether they delivered in Los Angeles County, Orange County, Ventura, or even as far south as San Diego.

The patients were asked about their income from allotments or other sources; about their medical and hospital bills, how much had been paid, how much they still owed, and how they planned to pay their bills. Other data were procured relative to the type and adequacy of care received. The persons doing the interviewing were alert for hardship cases and gave the patients every opportunity to discuss their financial difficulties. In addition, the wives of a number of civilians were visited who were in the same wards or similar accommodations to those of the servicemen's wives. Interpretations of hardship are variable, of course, but it was clear that the medical and financial needs of servicemen's families are adequately being taken care of in the Los Angeles area. The conclusions reached definitely do not indicate a need for a national program of care for servicemen's families, such as proposed by S. 1245 and S. 2337.

I would like to express the appreciation of the American Medical Association for this opportunity to appear before the Committee to present our views on this extremely important subject.

RESOLUTION TO BE PRESENTED TO HOUSE OF DELEGATES

The Secretary of the Association has received the following resolution on Negro physicians in North Carolina, which will be presented to the House of Delegates at the Chicago Session by a delegate of the Medical Society of the State of North Carolina:

WHEREAS, The members of the Medical Society of the State of North Carolina are anxious to maintain the cordial relations existing between the white and Negro physicians in North Carolina; and

WHEREAS, They recognize the advantages to the Negro physicians of membership in the American Medical Association; and

WHEREAS, At present it is not feasible, because of limits of space in the hotels of North Carolina, and also because of existing custom, to attempt to have joint meetings of both groups; and

WHEREAS, The Old North State Medical Society, which for fifty-three years has been the state organization of Negro physicians, has asked to be admitted "as a constituent association of the American Medical Association"; and

WHEREAS, The House of Delegates of the Medical Society of the State of North Carolina, at its annual meeting in May, 1951, voted to approve this request and sponsor the Old North State Medical Society as a constituent of the American Medical Association; therefore be it

Resolved, That the House of Delegates of the American Medical Association approve the recognition of the Old North State Medical Society as an affiliate of the Medical Society of the State of North Carolina, and also of the American Medical Association.

FEDERAL MEDICAL LEGISLATION

Hospital Transfers Between the VA and Defense Department

S. 2731, introduced by Senator Russell of Georgia, would authorize the transfer of hospitals and related facilities between the Veterans Administration and the Department of Defense without reimbursement. Under existing law, the Veterans Administration can acquire hospital facilities from the Department of Defense without transfer of funds, but the Defense Department may not acquire hospitals in this manner from the Veterans Administration. The bill is identical with H. R. 6724, previously reported.

Transfer of Indian Hospitals and Health Service

S. 2780, proposing to transfer the administration and health services for Indians and operation of Indian hospitals to the Public Health Service of the Federal Security Agency, was introduced by Senator Thye of Minnesota. It was introduced at the request of the Association of State and Territorial Health Officers. On introducing the bill, Senator Thye stated that none of the 62 hospitals now operated by the Bureau of Indian Affairs is recognized by the American Medical Association for the training of interns or otherwise as teaching hospitals. These Indian services are now under the Department of Interior.

Regulation of Fireworks

Senator O'Connor of Maryland introduced S. 2771, which would designate the Bureau of Mines in the Department of the Interior as the official agency for regulation of fireworks in interstate commerce. It is identical with H. R. 6722, previously reported.

Water Pollution

Representative Buckley of New York proposes to extend the duration of the Water Pollution Control Act in his bill H. R. 6856. The bill proposes the extension for three additional years of the Water Pollution Control Act, providing federal assistance to states through study, advice, and grants. The total amount of the grants is one million dollars annually.

STATE MEDICAL LEGISLATION

Arizona

Bill Introduced.—S. C. R. 11, proposes the submission to the people of a measure providing for the creation by the legislature of a department of public health and welfare.

California

Bills Introduced.—A. 13 and S. 4 propose to exempt from the sales tax the sale of uniforms dispensed on prescriptions filled by registered pharmacists in accordance with law.

Georgia

Bill Enacted.—H. 659 has become Act No. 889 of the Acts of 1952. It amends the uniform narcotic act by, among other things, providing for penalties for sales to a minor of any narcotic drug.

Kentucky

Bill Introduced.—H. 445, to amend the law relating to the state income tax, proposes to authorize taxpayers to deduct expenses paid during the taxable year for medical care of the taxpayer, his spouse or a dependent to the extent that such expenses exceed 5% of the taxpayer's adjusted income.

Massachusetts

Bill Introduced.—H. 2159, to amend the compulsory motor vehicle law, proposes that whenever an insurance company requires an insured to undergo medical examination following an accident, copies of the reports of such medical examination shall be furnished to the insurer and to the injured party.

The summary of federal legislation was prepared by the Washington Office of the American Medical Association and the summary of state legislation by the Bureau of Legal Medicine and Legislation.

Michigan

Bill Introduced.—S. 301, to amend the medical practice act, proposes regulations for the issuance of temporary annual licenses to practice medicine to doctors who are pursuing postgraduate study in the state and who meet certain qualifications.

Mississippi

Bills Introduced.—H. 531, proposes an appropriation to the state medical education board for the purpose of providing loans or scholarships for medical education of bona fide residents of the state. H. 579, proposes to require hospital commissions to establish uniform charges for care, treatment and hospitalization of charity patients and prohibits physicians from charging any fee for services rendered in connection with the treatment of charity patients.

New Jersey

Bills Introduced.—S. 40, proposes regulations for the licensing of physical therapists by the New Jersey board of medical examiners. S. 196, proposes to authorize any duly licensed physician to conduct a post-mortem examination upon the body of a deceased person if he first obtains the consent of any of the following persons who shall have assumed custody of the body for purposes of burial: parent, surviving spouse, child over the age of 18, guardian of the person or property of the deceased or next of kin. In the absence of any of the foregoing, any friend of the deceased who has assumed responsibility for burial or any other person charged by law with responsibility for burial may give such consent. S. 210, proposes to authorize boards of education to employ optometrists licensed to practice within the state who may be known as school vision examiners.

New York

Bills Introduced.—A. 2918, to amend the vehicle and traffic law, proposes to make it a misdemeanor for a person who is a habitual user of any narcotic drug to operate a motor vehicle or motorcycle while under the influence of such drug to a degree which renders him incapable of safely driving the vehicle. A. 2985, proposes regulations authorizing the state board of medical examiners to grant licenses to practice corrective therapy. A. 3008, to amend the education law, proposes the establishment of 500 state scholarships for nurses. A. 3009, proposes an appropriation to the education department for 300 additional scholarships for professional education in medicine and dentistry. A. 3025, proposes to make it grounds for revocation of a license for a physician, osteopath or physiotherapist to employ, hire, procure, induce, or aid or abet a person not licensed to practice one of those professions in the state, to so practice. A. 3045, to amend the education law, proposes to require optometrists to display their full names at the place where they practice. A. 3090, proposes the creation in the department of health of a division of narcotic control. A. 3147, proposes the creation within the department of health of an adult hygiene and geriatrics program designed to improve and protect the health and vitality of middle aged and elderly citizens of the state. A. 3193, proposes to require every physician to give notice to the health officer of the county, city, town, or village where such person resides of every case of unlawful narcotic use or addiction now under his care. A. 3198, proposes the creation of a temporary state commission to study the problem of sex deviation and to make recommendations concerning the solution thereto. S. 2313, proposes to make it the duty of every attending or consulting physician to report to the state department of health promptly the name and if possible the address of any person under treatment when it appears that such person is an habitual user of any narcotic drug. S. 2709, proposes the creation in the department of health of a permanent hospital survey and planning commission. S. 2717, proposes the creation of regional rehabilitation centers for alcoholics, to provide complete health patient service, including medical and psychiatric diagnosis and care, as well as rehabilitative social case work and therapy. S. 2834, proposes to authorize injured employees to be treated by duly registered and licensed podiatrists and to choose for such treatment any such podiatrist authorized by the chairman to render podiatry care.

Rhode Island

Bills Introduced.—H. 753, proposes to authorize the director of social welfare to appoint a chiropodist to give attention to disorders of the feet of inmates in institutions under the control of the state. H. 759 proposes to authorize the superintendent of schools to cause examinations to be made of school children for the purpose of guarding against outbreaks of infantile paralysis. Such examinations may include examinations of the leg and pedal extremities of children by physician, school nurses, or other licensed practitioners. No such examination shall be made of any child who presents a written statement signed by his parent or guardian stating that such examination should not be made because of religious beliefs or some other reasonable objection on the part of the parent or guardian.

Virginia

Bill Enacted.—S. 189 has become Ch. 143 of the Laws of 1952. It amends a law relating to medical scholarships by providing, among other things, that recipients of such scholarships shall insure their life for the benefit of the school awarding the scholarship in a sum equal to the value of the scholarship awarded to him.

MEDICAL NEWS

ALABAMA

Annual Clinical Society Meeting.—The John A. Andrew Clinical Society will conduct its 39th annual clinic at the Tuskegee Institute April 8-13. Fifty, or about half of the guest essayists and clinicians, are from outside the state. The society will memorialize the late Dr. John A. Kenney, founder and first president; the late Dr. Roy B. Kracke, dean of the Medical College of Alabama; and the late Dr. Charles Drew, professor of surgery, Howard University College of Medicine, Washington, D. C.

State Medical Meeting in Montgomery.—The Medical Association of the State of Alabama will hold its annual session at the Whitley Hotel, Montgomery, April 17-19 under the presidency of Dr. T. Brannon Hubbard of Montgomery. Out-of-state speakers include:

- Franklin L. Payne, Philadelphia, Care of Postmenopausal Patients.
- Robert B. McIver, Jacksonville, Fla., Plastic Surgery of the Renal Pelvis.
- Edward G. Waters, Jersey City, N. J., Medical and Surgical Therapy of Birth Hemorrhage.
- Richard B. Cattell, Boston, The Jerome Cochran Lecture, Carcinoma of the Colon and Rectum.
- James E. Scarborough Jr., Atlanta, Management of Cancer in the Neck.
- John B. Youmans, Nashville, Tenn., Macrocytic Anemia.
- Hugh F. Hare, Boston, X-Rays for Backache.
- Francis F. Schwentker, Baltimore, Modern Therapy of Rheumatic Fever.

CALIFORNIA

Social Hygiene Day.—The American Social Hygiene Association and the Venereal Disease Council of the City and County of Los Angeles will sponsor a regional conference in observance of National Social Hygiene Day April 23. Anton J. Carlson, Ph.D., Chicago, will speak on "Can Syphilis and Gonorrhea Be Eliminated from the Human Race?" The William Freeman Snow Medal will be presented to Ernest Boyd MacNaughton, president of Reed College, Portland, Ore., for distinguished service to humanity. Mr. MacNaughton is president and trustee of the Northwest Hospital Service and a vice-president of the American Social Hygiene Association.

Survey Course for General Practitioners.—This course is being presented April 14-18 by the University of Southern California Medical Extension Education at the Los Angeles County Hospital (Medical Unit) and the Childrens Hospital. It will consist of lectures, demonstrations, clinics, and staff conferences. Emphasis will be placed on new techniques, the use of new drugs, and new concepts in diagnosis and treatment. The American Academy of General Practice will recognize this course as formal training for those attending. The fee is \$50. The fee for fewer than five days will be \$10 per day. Information may be obtained from the University of Southern California Medical Extension office, 1200 N. State St., Los Angeles 33.

Course in Diagnostic Radiology.—Instruction in the usual radiographic procedures that can be performed in general office practice will be offered in a course in diagnostic radiology that the University of California Extension and the University of California School of Medicine will hold April 16-18 at the General Medical and Surgical Hospital, Veterans Administration Center, Los Angeles. Procedures in performing radiographic examinations will be stressed, as well as differential diagnoses to be considered in film interpretation. Requests for information concerning the course should be made to Dr. Thomas H. Sternberg, Head of Postgraduate Instruction, Medical Extension, University of California, Los Angeles 24. The course is open only to graduates of approved medical schools, and the fee is \$50.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

CONNECTICUT

Conferences at Institute of Living.—The 18th annual series of conferences at the Institute of Living has been announced. The four lectures are as follows:

- March 25, Main Causes of Difficulties Met with in Psychotherapy, Gregory Zilboorg, New York.
- April 8, Experimental Neuroses, Howard Scott Liddell, Ph.D., Ithaca, N. Y.
- April 22, Problem of Insight, Lawrence S. Kubie, New York.
- April 29, Psychotherapy of Psychoses, Elvin V. Semrad, Boston.

FLORIDA

Cancer Institute at Miami.—The Cancer Cytology Center of the Dade County Cancer Institute, Miami, an affiliate of the Medical Research Foundation of Dade County in Miami, announces a seminar for physicians to be held at the institute April 21-25, preceding the annual convention of the Florida Medical Association. The seminar on cancer cytology will also include a conference on carcinoma in-situ. Instruction will be under the supervision of Dr. J. Ernest Ayre, director of the institute, and the research staff. The general course of instruction in cancer diagnosis and cytology will include lectures, demonstrations, and symposiums. Interested physicians should direct their inquiries to the Director of the Dade County Cancer Institute at 1155 N. W. 14th St., Miami. Applications for registration, limited to 35 physicians, will be accepted through April 19.

ILLINOIS

Revise Quarantine Regulations.—A committee of public health officers in Illinois is drafting revisions of the rules and regulations for the control of communicable diseases in the state. The final draft is now being studied, and it will be several weeks before new rules can be made official.

Chicago

Personal.—Dr. Meyer A. Perlstein has been holding cerebral palsy clinics in Yakima, Seattle, Spokane, and Tacoma, Wash., sponsored by the Washington Society for Crippled Children and Adults. He also addressed medical students at the University of Washington School of Medicine.

Society Meeting.—At the meeting of the North Side Branch of the Chicago Medical Society at 8 p. m. April 3 at the Drake Hotel, Dr. Kenneth G. Kohlstaedt, director of the Lilly Laboratory for Clinical Research, Indianapolis, has been invited to speak on "Use of Ion Exchange Resins in Treatment of Edema."

Professor Leaves University for General Practice.—Dr. Henry G. Poncher, full time professor of pediatrics and head of the department at the University of Illinois College of Medicine, resigned his university appointment Aug. 31 to enter private practice in the community in which he resides, Valparaiso, Ind. Dr. Poncher will devote his time to a general family type of practice, excluding obstetrics and surgery. He also has accepted a part-time position as medical director of Valparaiso University, and as a visiting professor in human biology at that school. He plans to continue to serve in several national appointive positions that he holds, including the position of secretary-treasurer of the American Board of Pediatrics. Dr. Poncher has been associated with the University of Illinois since 1928. He was the first member of the faculty to receive two Raymond B. Allen Instructorship Awards in the same year. The award is designed to honor excellency in individual instruction rendered by faculty members to students.

INDIANA

Dr. Bahr Retires.—Dr. Max A. Bahr brought to a close on March 1 a service of 54 years with the Central State Hospital in Indianapolis. During about half of that time he had been superintendent and chief administrative officer. Presidents of state and local medical associations, the mayor of Indianapolis, and several state officials honored Dr. Bahr at a dinner Jan. 10.

IOWA

Personal.—Dr. Hermann M. Burian, formerly of Boston, has joined the staff of the department of ophthalmology at the State University of Iowa College of Medicine, Iowa City, as an associate professor.

State Medical Meeting in Des Moines.—The Iowa State Medical Society will hold its annual meeting at the Hotel Fort Des Moines in Des Moines April 27-30 under the presidency of Dr. Donald C. Conzett, Dubuque. Out-of-state speakers include:

- Henry L. Williams, Rochester, Minn., Practical Office Treatment of Menière's Disease.
- Russell J. Blattner, Houston, Texas, Cutaneous Manifestations of Viruses.
- Edgar V. Allen, Rochester, Minn., What Can Be Done About Hypertension?
- Robert A. Moore, St. Louis, Residency Training as an Educational Activity.
- Raymond J. Jackman, Rochester, Minn., Carcinoma Prevention Applied to the Large Intestine.
- Foster Matchett, Denver, Should I Call an Orthopedic Surgeon?
- Philip Thorek, Chicago, Jaundice.
- Edward J. McCormick, Toledo, Ohio, subject to be announced.
- William Malamud, Boston, Psychiatric Aspects of Geriatrics.
- John W. Harris, Madison, Wis., Prenatal Care—Accomplishments and Failures.
- Grover C. Penberthy, Detroit, Surgical Problems of the Newborn and Infant.

In addition to section meetings, several state societies and the woman's auxiliary will hold meetings and luncheons in conjunction with the state meeting.

MARYLAND

Halsted Centennial Gifts.—A bronze bust of Dr. William Stewart Halsted, the work of Vladimar Fortunato, was presented to the department of surgery of which he was first head in 1889 at the Johns Hopkins Hospital, at the Halsted Centennial meeting in Baltimore Feb. 7 (*THE JOURNAL*, Feb. 16, p. 561). Presentation was made by Dr. William F. Reinhoff Jr., associate professor of surgery at Johns Hopkins University. The bust, completed several months after Halsted's death in 1922, was given to Dr. Reinhoff in 1924 by Fortunato. Dr. Marcus M. Ravitch presented a gavel to the Society of University Surgeons on behalf of the Hopkins Department of Surgery. The gavel was fashioned from wood taken from Halsted's surgical amphitheatre and the staircase leading to his office. Dr. Emile F. Holman, chairman of the department of surgery at Stanford University School of Medicine, San Francisco, was chairman of the Centennial Committee. He was the last resident in surgery to serve under Dr. Halsted.

MASSACHUSETTS

Hospital Evening Lectures.—The House Officers' Association of the Boston City Hospital will present the following remaining programs in their evening lecture series:

- April 1, Mechanical Aspects of Urine Formation in Health and Disease, Stanley E. Bradley, New York.
- April 10, Problem of Food Intoxications with Special Reference to Botulism, Karl F. Meyer, Ph.D., San Francisco.
- April 15, Investigative Studies with Local Use of Steroids with Special Reference to Compound F, Leon Goldman, Cincinnati.

The programs are being held at 7 p. m. at the New Cheever Amphitheatre of the Dowling Building at Boston City Hospital. Interested persons are invited.

MICHIGAN

Narcotic Violation.—Dr. James M. Schuele, Au Gres, pleaded guilty to an indictment charging violation of the federal narcotic law on Dec. 28, 1951, at Bay City and was placed on probation for four years.

Sewage Service Personnel to be Licensed July 1.—The law now requires that persons, including partnerships, associations and corporations, engaged in servicing and cleaning of septic tanks, seepage pits, and cesspools must be licensed and bonded by the state commissioner of health in order to operate in Michigan after July 1. Instructions for obtaining a license and application forms can be procured from the Michigan Department of Health.

MISSOURI

Annual State Medical Meeting in St. Louis.—The Missouri State Medical Association will hold its annual meeting at the Hotel Jefferson, St. Louis, March 31 to April 2 under the presidency of Dr. C. Edgar Virden, Kansas City. The program includes symposiums on medicine, obstetrics, surgery, and pediatrics. Out-of-state speakers will be as follows:

- Walter C. Alvarez, Chicago, Why Some People Are So Terribly Nervous.
- Charles R. Rountree, Oklahoma City, Management of Fractures of the Patella.
- Hans P. Popper, Chicago, Hepatitis: Differential Diagnosis by Laboratory Studies.
- Gershom J. Thompson, Rochester, Minn., Treatment of Cancer of the Urinary Bladder with Particular Reference to the Selection of Operation.
- Robert L. Sanders, Memphis, The Gallbladder and Duct Problems.

There will be round table luncheons on Monday and Tuesday. At the banquet on Tuesday Dr. Louis H. Bauer, Hempstead, N. Y., President-Elect of the American Medical Association, will speak on "Problems Facing the Medical Profession." Several medical and allied organizations will meet preceding or concurrently with the association. Scientific and technical exhibits will be on display.

NEW JERSEY

Institute in Psychiatry and Neurology.—The second annual Institute in Psychiatry and Neurology will be held at the Veterans Administration Hospital, Lyons, on April 16. Among the guest lecturers will be Dr. Harvey J. Tompkins, chief, psychiatry and neurology division, Veterans Administration; Dr. Daniel Blain, medical director, American Psychiatric Association, and Dr. Winfred Overholser, superintendent, St. Elizabeth's Hospital, all of Washington, D. C.; Dr. Stephen P. Jewett, professor of psychiatry, New York Medical College, Flower and Fifth Avenue Hospitals; Dr. Samuel Brock, professor of neurology, New York University College of Medicine; Dr. Edward G. Billings, associate clinical professor of psychiatry, University of Colorado School of Medicine, Denver; Dr. D. Ewen Cameron, director, Allan Memorial Institute of Psychiatry, Montreal, Canada, and Dr. Frederick H. Allen, clinical professor of psychiatry, University of Pennsylvania School of Medicine, Philadelphia. There will also be six clinical demonstrations and ten medical exhibits by the hospital staff. The registration fee is \$1. Attendance of all interested professional personnel will be welcomed. Information may be obtained from Dr. Crawford N. Baganz, Manager, Veterans Administration Hospital, Lyons, N. J.

NEW YORK

Fraternity Lecture at Syracuse.—Dr. Harry Eagle, chief of experimental therapeutics of the Microbiological Institute, National Institutes of Health, Bethesda, Md., will speak for the Alpha Omega Alpha, national honorary medical fraternity, March 28 at 8:30 p. m. at the State University of New York College of Medicine at Syracuse. His topic will be "Factors Modifying the Therapeutic Effects of the Antibiotics."

County Society Begins TV Program.—The Medical Society of the County of New York inaugurated its series of television programs, "Here's to Your Health," in February. The first telecast presentation in documentary drama form over NBC on a sustaining basis was devoted to poliomyelitis and originated in the Institute of Physical Medicine and Rehabilitation of the New York University-Bellevue Medical Center. The second program featured heart disease. Future telecasts will be on cancer, high blood pressure, diabetes, and arthritis.

New York City

Biggs Memorial Lecture.—The Hermann M. Biggs Memorial Lecture, which is held annually in Hosack Hall at the New York Academy of Medicine under the auspices of the Committee on Public Health Relations, will be delivered at 8:30 p. m. April 3 by Dr. Erich Lindemann, associate professor in mental health, Harvard Medical School, Boston. The subject will be "Mental Health in a Community Health Program." The lecture is open to the public.

Seventh Harvey Lecture.—Dr. Louis B. Flexner, professor of anatomy, University of Pennsylvania School of Medicine, Philadelphia, delivered the seventh Harvey Lecture of the current series at the New York Academy of Medicine on March 20. Dr. Flexner spoke on "Development of the Cerebral Cortex: a Cytological, Functional and Biochemical Approach."

PENNSYLVANIA

Twenty-Four Hour Emergency Call Service.—The Medical Society of the State of Pennsylvania in reporting that 56 areas in 31 counties of the state now have 24 hour emergency medical call service urges the cooperation of all county medical societies to establish such services. Counties completely covered are Philadelphia, Lackawanna, Adams, Delaware, and Montgomery.

Philadelphia

Society News.—The Philadelphia Interstate Association of Industrial Medicine at its March 27 meeting will hear Dr. Francis X. Sweeney speak on "Sensible Use of Physiotherapy in an Industrial Dispensary." The meeting will be held in the Philadelphia County Medical Society building.

Solis-Cohen Memorial Lecture.—Dr. Ephraim Shorr, associate professor of medicine at Cornell University Medical College, New York, will deliver the annual Dr. Solomon Solis-Cohen Memorial Lecture at the auditorium of Mills Neurological Building March 27 at 8 p. m. He will speak on "The Role of Vasoactive Principles of Hepatic and Renal Origin in Hypertension." This is to be a scientific meeting of the medical staff of the city department of health and Philadelphia General Hospital.

TEXAS

University Appointment.—Isaac D. Welt, Ph.D., has been appointed assistant director and principal scientist of the Radioisotope Unit, Veterans Administration Hospital, Houston, and assistant professor of biochemistry at Baylor University College of Medicine. Dr. Welt was formerly on the staff of the division of nutrition and physiology of the Public Health Research Institute of the City of New York, Inc.

WEST VIRGINIA

Medical Meetings.—The first meeting arranged by the state medical association's committee on medical education for 1952 will be held at the Stonewall Jackson Hotel in Clarksburg April 17. The second meeting is scheduled for Oak Hill on May 22. At the Clarksburg meeting, opening at 10 a. m., the theme will be "Acute Pulmonary Diseases." The basic science faculty of the West Virginia University School of Medicine will present the fundamental concepts at the morning session; the clinical aspects will be presented at the afternoon session by two guest speakers.

ANAL ZONE

Annual Association Meeting.—The Medical Association of the Isthmian Canal Zone held its annual meeting at Gorgas Memorial Laboratory, Panama City, Jan. 15. Guests of the society included Drs. Don Brewster, Holdredge, Neb., Henry W. Daine, San Juan, Puerto Rico, and Mark K. Nettles, Lima, Peru. Dr. Norman W. Elton, Ancon, was elected president and Dr. Irving J. Strumpf, Ancon, secretary. The program included the following papers presented by the surgical section of Gorgas Hospital:

Subclavian Aneurysm—Surgical Treatment Case Report, Eugene D. Eрман.

Operative Repair of Hair Lip, Earl C. Lowry.

Total Adrenalectomy, Richard W. Satterthwaite.

PUERTO RICO

Appoint Temporary Dean of Puerto Rican School.—Dr. Donald S. Martin, dean of the University of Puerto Rico School of Medicine, has resigned effective April 20, and Dr. Harold W. Brown, director, School of Public Health of Columbia University, has been designated dean of the University of Puerto Rico School of Medicine, to serve until a permanent dean is selected. Dr. Brown was active in the early development of the medical school in Puerto Rico. He will continue as director of the School of Public Health of Columbia University.

GENERAL

Dr. Burn to Address Dinner Meeting.—Dr. J. H. Burn, Oxford, England, will speak at the dinner of the American Society for Pharmacology and Experimental Therapeutics at 7 p. m. April 16 at the Hotel Statler, New York.

Society News.—Dr. Robert R. Commons, assistant clinical professor of medicine at the University of Southern California School of Medicine, Los Angeles, was elected chairman of the western section of the American Federation of Clinical Research during the annual meeting at Carmel, Calif., Jan. 24.

Tri-State Postgraduate Meeting.—The Northern Tri-State Post Graduate Medical Association, which includes Indiana, Ohio, and Michigan, will hold its annual meeting on the campus of the University of Notre Dame in South Bend, Ind., April 15. All doctors are invited. For reservations address Dr. Joseph Lang, 730 J. M. S. Building, South Bend.

Booklet on Chronic Disease.—"Steps Toward Prevention of Chronic Disease," a summary report of the National Conference on Preventive Aspects of Chronic Disease held in March 1951, in Chicago, has been published by the Health Publications Institute, Inc., Raleigh, N. C., and is being sold by that organization for 50 cents a copy. The complete proceedings of the conference will not be published for several months.

Immunologists Meeting.—The American Association of Immunologists will hold its annual meeting at the Hotel Statler and the New Yorker in New York April 15-18 under the presidency of Dr. Colin M. MacLeod, New York. The program includes a symposium on "Antigenic Variation of Influenza Viruses and Its Importance in Vaccination," and another on uses and value of human gamma globulin. The Friday morning program will be devoted to tuberculosis and allergy.

Cancer Society Seeks Sixteen Million Dollars.—The American Cancer Society will conduct its 1952 Cancer Crusade for \$16 million in April. The money is to be used to forward programs of research, education, and patient services. Since 1945 the society has put about \$20,500,000 into cancer research. This year it has awarded over \$1.5 million to 265 grant-in-aid projects. An additional million and a half was awarded to 32 universities and hospitals conducting integrated research programs, and over \$350,000 in a fellowship training program.

Multiple Sclerosis Society.—Dr. Hans H. Reese, Madison, Wis., president-elect of the American Neurological Association, has been appointed chairman of the medical advisory board of the National Multiple Sclerosis Society for a two year term. Dr. Reese is professor of neurology and psychiatry of the University of Wisconsin Medical School, Madison. Newly appointed vice-chairman of the board is Dr. Richard M. Brickner, assistant clinical professor of neurology, Columbia University College of Physicians and Surgeons, New York. Dr. Brickner is also associated with Mount Sinai Hospital in New York. Dr. Tracy J. Putnam, formerly chairman of the medical advisory board, has been appointed honorary chairman.

Forty-One Million Children.—Children in the United States increased in number by 8,000,000 during the 1940's, which was the largest gain in a single decade in the country's history, Metropolitan Life Insurance Company statisticians report. By 1950, there were 41,000,000 persons less than 15 years old, an all time high. During the 10 year period the number of children increased at a substantially higher rate than the population as a whole, the rate of growth being 24.1% for the children as compared with 14.5% for the entire population. By contrast, in the 1930's the child population declined, despite an increase in the population as a whole. The decline in the child population during that decade was so rapid that the number of American youngsters by 1940 was actually smaller than in 1920, and there were fewer under the age of 5 than in 1910.

CANADA

Dr. Chute to Head Department.—Dr. Andrew L. Chute, Toronto, has been appointed professor of pediatrics and head of the pediatrics department at the University of Toronto Faculty of Medicine. He will also serve as physician-in-chief of the department of pediatrics at the Hospital for Sick Children.

EXAMINATIONS AND LICENSURE

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 24-26, 1952. Sec., Dr. D. G. Gill, 537 Dexter Ave., Montgomery 4.

ALASKA: * *Examination.* Juneau. On application in other towns where there are board members. *Reciprocity.* On application. Sec., Dr. W. M. Whitehead, Box 140, Juneau.

ARIZONA: * *Examination.* Phoenix, April 15-17. *Reciprocity.* Phoenix, April 19. Sec., Dr. J. H. Patterson, 316 W. McDowell St., Phoenix.

ARKANSAS: * *Examination. Regular.* Little Rock, June 5-6. Sec., Dr. Joe Verser, Harrisburg. *Homoeopathic.* Little Rock, June 10-11. Sec., Dr. Carl S. Bungari, 105 N. 14th St., Fort Smith. *Eclectic.* Little Rock, June 5-6. Sec., Dr. Frank C. Smith, 2301 Broadway, Little Rock.

CALIFORNIA: *Written.* Los Angeles, Feb. 18-21; San Francisco, June 23-26; Los Angeles, Aug. 18-21; Sacramento, Oct. 20-23. Application must be received at least two weeks prior to date of examination. *Oral for Reciprocity Applicants.* San Francisco, June 21; Los Angeles, Aug. 16; San Francisco, Nov. 8. Applicants are requested not to arrange to come to an oral examination until they receive notice from the Credentials Committee. *Oral and Clinical for Foreign Medical School Graduates.* San Francisco, June 22; Los Angeles, Aug. 17; San Francisco, Nov. 9. Sec., Dr. Frederick N. Scatena, 1020 N St., Sacramento.

COLORADO: * *Examination.* Denver, June 10-12. Final date for filing application is May 12. *Reciprocity.* Denver, April 8. Final date for filing application was Mar. 10. Sec., Dr. Samuel H. Brown, 831 Republic Bldg., Denver.

DELAWARE: Dover, July 8-10. Sec., Dr. Joseph S. McDaniel, 229 South State St., Dover.

FLORIDA: * *Examination.* Jacksonville, June 29-July 1. Sec., Dr. Homer L. Pearson, 701 Dupont Bldg., Miami.

GEORGIA: Atlanta and Augusta, June. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta 3.

GUAM: The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Ex. Sec., Dr. Austin W. Matthis, Agaña.

HAWAII: *Examination.* Honolulu, July 14-17. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

IDaho: Boise, July 14-16. Sec., Mr. Armand L. Bird, 305 Sun Bldg., Boise.

ILLINOIS: * *Examination.* Chicago, April 1-3, June 24-26 and Oct. 7-9. Supt. of Regis., Mr. Charles F. Kervin, Capitol Bldg., Springfield.

INDIANA: Indianapolis, June 1952. Sec., Dr. Paul R. Findall, 1138 K of P Bldg., Indianapolis 4.

IOWA: * *Examination.* Iowa City, June 9-11. Sec., Dr. M. A. Royal, 506 Fleming Bldg., Des Moines.

KANSAS: Kansas City, June 4-5. Sec., Dr. O. W. Davidson, 864 New Brotherhood Bldg., Kansas City.

KENTUCKY: * *Examination.* Louisville, June 3-5. Sec., Dr. Bruce Underwood, 620 S. Third St., Louisville.

MARYLAND: * *Examination.* Baltimore, June 17-20. Sec., Dr. Lewis P. Grundy, 1215 Cathedral St., Baltimore. *Homoeopathic.* Baltimore, June 17-18. Sec., Dr. John A. Evans, 6029 Bellona Ave., Baltimore.

MICHIGAN: * *Examination.* June. Sec., Dr. J. E. McIntyre, 100 W. Allegan St., Lansing 8.

MINNESOTA: Minneapolis, April 15-17. Sec., Dr. Julian F. DuBois, 230 Lowry Medical Arts Bldg., St. Paul 2.

MONTANA: Helena, April 1. Sec., Dr. S. A. Cooney, 214 Power Block, Helena.

NEBRASKA: * *Examination.* Omaha, June 16-18. Director, Mr. Husted K. Watson, Bureau of Examining Boards, Room 1009, State Capitol, Lincoln.

NEW JERSEY: * *Examination.* Trenton, June 17-20. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: * Santa Fe, April 14-15. Sec., Dr. Charles J. McGoey, Coronado Bldg., Santa Fe.

NORTH CAROLINA: * *Reciprocity.* Pinehurst, May 5. *Written.* Raleigh, June 16-19; *Reciprocity.* Raleigh, June 17. Sec., Dr. Joseph J. Combs, 716 Professional Bldg., Raleigh.

NORTH DAKOTA: * *Examination.* Grand Forks, July 9-11. *Reciprocity.* Grand Forks, July 12. Sec., Dr. C. J. Glaspel, Grafton.

OHIO: * *Examination.* Columbus, June 17-20. *Reciprocity.* Columbus, April 1. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus 15.

OKLAHOMA: * *Examination.* Oklahoma City, June 4-5. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON: * *Reciprocity.* Portland, April 18-19. *Examination.* Portland, July. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland.

RHODE ISLAND: * *Examination.* Providence, April 3-4. Sec., Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: * *Reciprocity.* Columbia, April 7. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA: * Rapid City, July 15. Sec., Dr. C. B. McVay, Yankton Clinic, Yankton.

TENNESSEE: * *Examination.* Memphis, March 26-27. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis.

TEXAS: Fort Worth, June 19-21. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth.

UTAH: * *Examination.* Salt Lake City, July. Asst. Dir., Mr. Frank E. Lees, 314 State Capitol Bldg., Salt Lake City 1.

VIRGINIA: * *Examination.* Richmond, June 12-14. *Reciprocity.* Richmond, June 11. Sec., Dr. K. D. Graves, 631 First St., S.W., Roanoke.

VIRGIN ISLANDS: St. Thomas, June 4-5. Sec., Dr. Earle M. Rice, St. Thomas.

WEST VIRGINIA: Charleston, April 7-8. Sec., Dr. H. H. Dyer, State Office Bldg. No. 3, Charleston 5.

WASHINGTON: Seattle, July. Sec., Mr. Edward C. Dohm, Department of Licenses, Olympia.

WISCONSIN: * Milwaukee, July 8-10. Sec., Dr. A. G. Koehler, 46 Washington Blvd., Oshkosh.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: * *Examination.* On application. Juneau or other towns in Territory as decided by Board. *Reciprocity.* On application. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

ARKANSAS: * *Examination.* Little Rock, May 1-2. Sec., Mr. L. E. Gebauer, 1002 Donaghey Bldg., Little Rock.

DISTRICT OF COLUMBIA: * *Examination.* Washington, April 21-22. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Bldg., Washington, D. C.

FLORIDA: Gainesville, June 7. *Examination.* Sec., Mr. M. W. Emmel, Box 340, University of Florida, Gainesville.

OKLAHOMA: * *Examination.* Oklahoma City, April 14. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON: * *Examination.* Portland, June 7, Sept. 6 and Dec. 6. Sec., Dr. Charles D. Byrne, State Board of Higher Education, University of Oregon, Eugene.

SOUTH DAKOTA: Vermillion, June 13-14. Sec., Dr. Gregg M. Evans, 310 E. 15th St., Yankton.

TEXAS: Austin, April 18-19. *Examination.* Examination may also be given in Galveston, Dallas and Houston. Sec., Bro. Rapheal Wilson, 306 Nalle Bldg., Austin.

WISCONSIN: * *Examination.* Madison, April 5, and Milwaukee, June 7. Sec., Mr. W. H. Barber, Ripon College, Ripon.

* Basic Science Certificate required.

MEETINGS

ALABAMA, MEDICAL ASSOCIATION OF THE STATE OF, Montgomery, April 17-19. Dr. Douglas L. Cannon, 519 Dexter Ave., Montgomery, Secretary.

AMERICAN ACADEMY OF GENERAL PRACTICE, Atlantic City, N. J., March 24-27. Mr. Mac F. Cahal, 406 West 34th St., Kansas City 2, Mo., Executive Secretary.

AMERICAN ACADEMY OF NEUROLOGY, Brown Hotel, Louisville, Ky., Apr. 24-25. Dr. Francis M. Forster, 3800 Reservoir Rd. N.W., Washington, D. C., Secretary.

AMERICAN ACADEMY OF OBSTETRICS AND GYNECOLOGY, Cincinnati, April 1. Dr. Ralph A. Reis, 116 South Michigan Boulevard, Chicago 3, Secretary.

AMERICAN ASSOCIATION FOR THORACIC SURGERY, Dallas, Texas, May 8-10. Dr. Paul C. Samson, 2938 McClure St., Oakland 9, Calif., Secretary.

AMERICAN ASSOCIATION OF IMMUNOLOGISTS, New York, April 14. Dr. John Y. Sugg, 1300 York Ave., New York, Secretary.

AMERICAN ASSOCIATION OF PATHOLOGISTS AND BACTERIOLOGISTS, New York, April 10-12. Dr. Alan R. Moritz, 2085 Adelbert Road, Cleveland 6, Secretary.

AMERICAN ASSOCIATION OF RAILWAY SURGEONS, Drake Hotel, Chicago, April 1-3. Dr. Chester C. Guy, 5800 Stony Island Ave., Chicago 37, Secretary.

AMERICAN ASSOCIATION OF THE HISTORY OF MEDICINE, Kansas City, Kans., May 1-3. Dr. Iago Gaidston, 2 East 103d St., New York 29, Secretary.

AMERICAN COLLEGE OF ALLERGISTS, William Penn Hotel, Pittsburgh, April 7-9. Dr. Fred W. Wittich, 401 LaSalle Medical Bldg., Minneapolis 2, Secretary.

AMERICAN COLLEGE OF PHYSICIANS, Cleveland, April 21-25. Mr. E. R. Loveland, 4200 Pine St., Philadelphia 4, Executive Secretary.

AMERICAN COLLEGE OF SURGEONS, SECTIONAL MEETINGS: Minneapolis, Radisson Hotel, March 24-26. Dr. Harvey Nelson, 78 South 9th St., Minneapolis 2, Chairman.

Tucson, Ariz., Pioneer Hotel, April 7-9. Dr. Meade Clyne, 110 South Scott St., Tucson, Chairman.

Vancouver, B. C., Vancouver Hotel, March 31-April 4. Dr. J. Russell Neilson, 925 West Georgia St., Vancouver, B. C., Chairman.

AMERICAN CONGRESS ON OBSTETRICS AND GYNECOLOGY, Netherlands-Plaza Hotel, Cincinnati, March 31-April 4. Dr. Luella E. Nadelhoffer, 116 South Michigan Ave., Chicago 3, Secretary.

AMERICAN DERMATOLOGICAL ASSOCIATION, Broadmoor Hotel, Colorado Springs, Colo., Apr. 23-26. Dr. Louis A. Brunsting, 102 Second Ave. S.W., Rochester, Minn., Secretary.

AMERICAN ELECTROENCEPHALOGRAPHIC SOCIETY, Hotel Claridge, Atlantic City, N. J., May 10-11. Dr. John A. Abbott, Massachusetts General Hospital, Boston 14, Secretary.

AMERICAN FEDERATION FOR CLINICAL RESEARCH, Haddon Hall, Atlantic City, N. J., May 4. Dr. Stewart Wolf, 525 East 68th St., New York 21, Secretary.

AMERICAN GASTRO-ENTEROLOGICAL ASSOCIATION, Hotel Claridge, Atlantic City, N. J., May 2-3. Dr. Dwight L. Wilbur, 655 Sutter St., San Francisco 2, Secretary.

AMERICAN GASTROSCOPIC SOCIETY, Hotel Claridge, Atlantic City, N. J., May 2-3. Dr. H. Marvin Pollard, University Hospital, Ann Arbor, Mich., Secretary.

AMERICAN GOUTER ASSOCIATION, Chase Hotel, St. Louis, May 1-3. Dr. George C. Shivers, 100 East St. Vrain St., Colorado Springs, Colo., Secretary.

AMERICAN GYNECOLOGICAL SOCIETY, The Homestead, Hot Springs, Va., May 12-14. Dr. John I. Brewer, 104 South Michigan Ave., Chicago, Secretary.

AMERICAN HEART ASSOCIATION, Hotel Statler, Cleveland, April 17-20. Dr. William H. Bunn, 1775 Broadway, New York 19, Secretary.

AMERICAN NEUROLOGICAL ASSOCIATION, Hotel Claridge, Atlantic City, N. J., May 8-10. Dr. H. Houston Merritt, 710 West 168th St., New York 32, Secretary.

AMERICAN PEDIATRIC SOCIETY, Hotel Chamberlin, Old Point Comfort, Va., May 7-9. Dr. Aims C. McGuiness, 237 Medical Laboratories, Univ. of Pennsylvania, Philadelphia 4, Secretary.

AMERICAN PSYCHIATRIC ASSOCIATION, Atlantic City, N. J., May 12-16. Dr. R. Finley Gayle Jr., 6300 Three Chopt Rd., Richmond 21, Va., Secretary.

AMERICAN PSYCHOSOMATIC SOCIETY, The Drake, Chicago, March 29-30. Dr. Frederick C. Redlich, 551 Madison Avenue, New York 22, Secretary.

AMERICAN SOCIETY FOR CLINICAL INVESTIGATION, Atlantic City, N. J., May 5. Dr. William M. M. Kirby, Univ. of Washington School of Medicine, Seattle 5, Secretary.

AMERICAN SOCIETY FOR EXPERIMENTAL PATHOLOGY, New York, April 14-18. Dr. Russell L. Holman, 1542 Tulane Ave., New Orleans 12, Secretary.

AMERICAN SOCIETY FOR PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, Hotel Statler, New York, April 14-18. Dr. Carl C. Pfeiffer, 1835 W. Polk St., Chicago 12, Secretary.

AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, New York, April 14-18. Dr. Elmer H. Stotz, 260 Crittenden Blvd., Rochester, N. Y., Secretary.

AMERICAN SURGICAL ASSOCIATION, White Sulphur Springs, W. Va., Apr. 16-18. Dr. Nathan A. Womack, University Hospitals, Iowa City, Secretary.

AMERICAN VENEREAL DISEASE ASSOCIATION, Washington, D. C., May 1-2. Dr. William L. Fleming, 750 Harrison Ave., Boston 18, Secretary.

ARIZONA MEDICAL ASSOCIATION, Phoenix, April 30-May 3. Dr. Frank J. Milloy, 15 E. Monroe St., Phoenix, Secretary.

ARKANSAS MEDICAL SOCIETY, Little Rock, April 21-23. Dr. William R. Brooksher, 215 Kelley Bldg., Fort Smith, Secretary.

ASSOCIATION OF AMERICAN PHYSICIANS, Atlantic City, N. J., May 6-7. Dr. Henry Thomas Jr., 1201 North Calvert St., Baltimore 2, Secretary.

CALIFORNIA MEDICAL ASSOCIATION, Biltmore Hotel, Los Angeles, April 27-30. Dr. Albert C. Daniels, 450 Sutter St., San Francisco 8, Secretary.

CONNECTICUT STATE MEDICAL SOCIETY, Hartford, April 29-May 1. Dr. Creighton Barker, 160 St. Ronan Street, New Haven, Secretary.

FLORIDA MEDICAL ASSOCIATION, Hollywood, April 27-30. Dr. Samuel M. Day, P. O. Box 1018, Jacksonville, Secretary.

GEORGIA MEDICAL ASSOCIATION OF ATLANTA-BILTMORE HOTEL, Atlanta, May 12-14. Dr. David H. Poer, 875 West Peachtree St. N.E., Atlanta, Secretary.

HAWAII TERRITORIAL MEDICAL ASSOCIATION, Honolulu, May 1-4. Dr. I. L. Tilden, 510 S. Beretania St., Honolulu 13, Secretary.

INDUSTRIAL MEDICAL ASSOCIATION, Cincinnati, April 21-24. Dr. Edward C. Holmblad, 28 E. Jackson Blvd., Chicago 4, Managing Director.

IOWA STATE MEDICAL SOCIETY, Des Moines, April 28-30. Dr. Allan B. Phillips, 406 Sixth Avenue, Des Moines 9, Secretary.

JOHN A. ANDREW CLINICAL SOCIETY, Memorial Hospital, Tuskegee Institute, Ala., April 6-12. Dr. Eugene H. Dibble Jr., Memorial Hospital, Tuskegee Institute, Secretary.

KANSAS MEDICAL SOCIETY, Town House, Kansas City, April 27-May 1. Dr. Dale D. Vermillion, 512 New England Bldg., Topeka, Secretary.

LOUISIANA STATE MEDICAL SOCIETY, Shreveport, April 28-30. Dr. C. Grenes Cole, 1430 Tulane Ave., New Orleans 12, Secretary.

MARYLAND, MEDICAL AND CHIRURGICAL FACULTY OF THE STATE OF, Baltimore, April 28-30. Dr. George H. Yeager, 1211 Cathedral St., Baltimore 1, Secretary.

MID-CONTINENT PSYCHIATRIC ASSOCIATION, President Hotel, Kansas City, Mo., April 26-27. Dr. Paul Hines, 2625 W. Paseo, Kansas City, Mo., Secretary.

MISSISSIPPI STATE MEDICAL ASSOCIATION, Jackson, May 13-15. Mr. Roland B. Kennedy, 508 First Federal Bldg., Jackson, Executive Secretary.

MISSOURI STATE MEDICAL ASSOCIATION, Hotel Jefferson, St. Louis, March 30-April 2. Dr. H. E. Petersen, 634 North Grand Blvd., St. Louis 3, Secretary.

NEW MEXICO MEDICAL SOCIETY, Carlsbad, May 8-10. Dr. L. G. Rice Jr., 221 West Central Ave., Albuquerque, Secretary.

NORTH CAROLINA, MEDICAL SOCIETY OF THE STATE OF, Hotel Carolina, Pinehurst, May 5-7. Dr. Millard D. Hill, 203 Capitol Club Bldg., Raleigh, Secretary.

PIEDMONT PROCTOLOGIC SOCIETY, Charlotte, N. C., March 29-30. Dr. B. Richard Jackson, 224 Hillsboro St., Raleigh, N. C., Secretary.

POST GRADUATE INSTITUTE OF THE PHILADELPHIA COUNTY MEDICAL SOCIETY, Bellevue-Stratford Hotel, Philadelphia, April 1-4. Dr. Thomas M. Durant, 301 South 21st St., Philadelphia 3, Director.

RHODE ISLAND MEDICAL SOCIETY, Providence, May 6-8. Dr. Morgan Cutts, 106 Francis St., Providence 3, Secretary.

SOCIETY FOR PEDIATRIC RESEARCH, Old Point Comfort, Va., May 5-6. Dr. Sydney S. Gellis, 300 Longwood Ave., Boston 15, Secretary.

SOCIETY OF AMERICAN BACTERIOLOGISTS, Hotel Statler, Boston, April 27-May 1. Dr. Henry W. Scherp, 260 Crittenden Blvd., Rochester 20, N. Y., Secretary.

SOUTHEASTERN SECTION, AMERICAN UROLOGICAL ASSOCIATION, Boca Raton, Fla., April 2-5. Dr. Russell B. Carson, Sweet Bldg., Fort Lauderdale, Fla., Secretary.

TENNESSEE STATE MEDICAL ASSOCIATION, Andrew Johnson Hotel, Knoxville, April 7-9. Mr. V. O. Foster, 504 Doctors Bldg., Nashville 3, Executive Secretary.

TEXAS MEDICAL ASSOCIATION, Dallas, May 4-7. Dr. Sam N. Key Sr., 700 Guadalupe St., Austin 3, Secretary.

WESTERN ASSOCIATION OF INDUSTRIAL PHYSICIANS AND SURGEONS, Biltmore Hotel, Los Angeles, April 26. Dr. David D. Holaday, American Can Company, Third and 20th Sts., San Francisco 7, Secretary.

INTERNATIONAL

AUSTRALASIAN MEDICAL CONGRESS, Melbourne Victoria, Australia, Aug. 22-30. Dr. C. H. Dickson, Medical Society Hall, 426 Albert St., East Melbourne, Victoria, Australia, Hon. General Secretary.

COMMONWEALTH AND EMPIRE HEALTH AND TUBERCULOSIS CONFERENCE, Central Hall, London, England, July 8-13. Dr. J. H. Harley Williams, Tavistock House North, Tavistock Sq., London, W.C.1, England, Secretary General.

CONGRESS OF THE INTERNATIONAL DIABETES FEDERATION, Leyden, Netherlands, July 7-12. Dr. F. Gerritzen, 33, Prinsegracht, The Hague, Netherlands, Secretary.

EUROPEAN CONGRESS OF CARDIOLOGY, University of London, Bloomsbury, W.C.1, England, Sept. 10-12. Dr. K. Shirley Smith, 35 Wimpole St., London, W.1, England, Secretary.

EUROPEAN SOCIETY OF CARDIOVASCULAR SURGERY, Strasbourg, France, Oct. 3-4. Sir James Learmonth, Department of Surgery, University New Buildings, Edinburgh 8, Scotland.

INTERAMERICAN CARDIOLOGICAL CONGRESS, Buenos Aires, Argentina, Aug. 31-Sept. 7. Dr. Blas Moia, Larrea 1132, Buenos Aires, Argentina, Secretary-General.

INTER-AMERICAN CONGRESS OF PUBLIC HEALTH, Havana, Cuba, Sept. 27-Oct. 1. Pan-American Sanitary Bureau, 2001 Connecticut Ave., Washington, D. C.

INTER-AMERICAN CONGRESS OF RADIOLOGY, Mexico City, Mexico, Nov. 2-6. Dr. Guido Torres Martinez, Marsella No. 11, Mexico, D.F., Secretary-General.

INTERNATIONAL COLLEGE OF SURGEONS, Madrid, Spain, May 20-24. Dr. Max Thorek, 850 West Irving Park Road, Chicago, Ill., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF BIOCHEMISTRY, Paris, France, July 21-27. Prof. Jean Courtois, 4, Avenue de l'Observatoire, Paris 6^e, France, Secretary.

INTERNATIONAL CONGRESS OF COMPARATIVE PATHOLOGY, Madrid, Spain, May 4-11. Prof. Carda-Aparici, Calle Fernando VI.8, Madrid, Spain, Secretary.

INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY, London, England, July 21-26. Dr. Gordon B. Mitchell-Heggs, 5, Lisle St., London, W.C.2, England, General Secretary.

INTERNATIONAL CONGRESS ON DIABETES, Leyden, The Netherlands, July 7-12. Dr. F. Gerritzen, 33, Prinsegracht, The Hague, Netherlands.

INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST, Rio de Janeiro, Brazil, Aug. 24-30. Mr. Murray Kornfeld, 112 East Chestnut St., Chicago 11, Illinois, Executive Secretary.

INTERNATIONAL CONGRESS OF HAEMATOLOGY, Mar del Plata, Argentina, Sept. 21-26. Dr. Carlos Reussi, Anchorena 1710, Buenos Aires, Argentina, Secretary.

INTERNATIONAL CONGRESS OF HEALTH TECHNICIANS, Palais de la Mutualite, Paris, France, June 9-14. Secretariat General, 6 Square Desaix, Paris XV^e, France.

INTERNATIONAL CONGRESS OF THE HISTORY OF MEDICINE, Nice-Cannes, France, and Monaco, Sept. 8-18. Dr. F. A. Sondervorst, 124 Avenue des Allies, Louvain, Belgium, Secretary-General.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Friends House, London, N.W.1, Eng. Sept. 15-18. Sir Harold Boldero, 12 Pall Mall East, London, S.W.1, England, Secretary.

INTERNATIONAL CONGRESS ON MEDICAL RECORDS, London, England, Sept. 7-12. Miss Gwen Perkins, 120 C Street S.E., Washington, D. C., Chairman.

INTERNATIONAL CONGRESS OF MEDICINE AND SPORT, Paris, France, May 29-June 1. Prof. Chailley-Bert, 1 rue Lacretelle, Paris 15^e, France, Chairman.

INTERNATIONAL CONGRESS ON NEUROPATHOLOGY, Rome, Italy, Sept. 8-13. Dr. Armando Ferraro, 722 W. 168th St., New York, N. Y., U. S. A., Secretary General.

INTERNATIONAL CONGRESS OF OTO-NEURO-OPHTHALMOLOGY, Lisbon and Estoril, Portugal, April 22-26. Prof. Diogo Furtado, Servico de Neurologia, Hospital dos Capuchos, Lisbon, Portugal, General Secretary.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE, London, England, July 14-19. Dr. A. C. Boyle, 45, Lincoln's Inn Fields, London, W.C.2, England, Hon. Secretary.

INTERNATIONAL CONGRESS OF PHYSIOPATHOLOGY OF ANIMAL REPRODUCTION AND ARTIFICIAL INSEMINATION, Copenhagen, Denmark, July 7-10. Prof. Ed. Sorensen, The Royal Veterinary and Agricultural College, Bülowsvej 13, Copenhagen V, Denmark.

INTERNATIONAL CONGRESS FOR THERMALISM AND CLIMATOTHERAPY, Nice-Cannes, France, April 3-8.

INTERNATIONAL CONGRESS OF UROLOGY, New York, N. Y., U. S. A., Sept. 15-18. Dr. John A. Taylor, 2 East 54th St., New York, N. Y., U. S. A., Secretary-General.

INTERNATIONAL SOCIETY OF GEOGRAPHIC PATHOLOGY, Liège, Belgium, July 15-18. Dr. Fred C. Roulet, Habelstr. 24, Basei, Switzerland, Secretary General.

INTERNATIONAL UNION AGAINST TUBERCULOSIS, Rio de Janeiro, Brazil, Aug. 24-27. Prof. Etienne Bernard, 66 Blvd. St. Michel, Paris 6^e, France, Secretary-General.

NEURORADIOLOGIC SYMPOSIUM, Stockholm, Sweden, Sept. 17-20. Docent Åke Lindbom, Symposium Neuroradiologicum, Serafimerlasarettet, Stockholm K., Sweden, Secretary.

PAN-AMERICAN CONGRESS OF GASTROENTEROLOGY, Mexico City, D.F., May 11-17. Dr. R. Flores-Lopez, Calle Dr. Balmis, No. 148, Mexico City, D.F., Secretary.

PAN-EUROPEAN CONGRESS OF GASTROENTEROLOGY, Bologna, Florence and Rome, Italy, April 20-26. Prof. Guido Bassi, Policlinic of St. Orsola, Bologna, Italy, Secretary.

WORLD MEDICAL ASSOCIATION, Athens, Greece, Oct. 12-16. Dr. Louis H. Bauer, 2 East 103d St., New York 29, N. Y., Secretary General.

DEATHS

Hughes, Byron James, Winnebago, Wis.; born in Wyocena, Wis., April 28, 1904; University of Wisconsin Medical School, Madison, 1931; preceptor at his alma mater; chairman of the medical section, department of Veterans Affairs; psychiatrist, medical review board, Selective Service from 1943 to 1947; specialist certified by the American Board of Psychiatry and Neurology; past president of the Winnebago County Medical Society and the Milwaukee Neuropsychiatric Society; served as vice-speaker and speaker of the House of Delegates of the State Medical Society of Wisconsin; member of the American Medical Association, American Psychiatric Association, American Association on Mental Deficiency, Wisconsin Society of Mental Health, American College of Physicians, and the Wisconsin Anti-Tuberculosis Association; lecturer in psychiatry from 1934 to 1942 at Mercy Hospital School of Nursing, Oshkosh, where he was a council member; consultant, Alexian Brothers Hospital, Oshkosh; senior physician from 1933 to 1936, institutional physician, 1936-1937, assistant superintendent and clinical director from 1937 to 1939, acting superintendent, 1939-1940, and since 1940 superintendent, Winnebago State Hospital; chairman, department of psychiatry, Mercy Hospital in Oshkosh, where he died Jan. 15, aged 47, of cerebral hemorrhage and hypertensive cardiovascular disease.

Phelps, Olney Draper * Worcester, Mass.; born in Brattleboro, Vt., Jan. 22, 1881; Dartmouth Medical School, Hanover, N. H., 1907; specialist certified by the American Board of Urology; an Associate Fellow of the American Medical Association; member of the American Urological Association; fellow of the American College of Surgeons; surgeon, Holden District Hospital in Holden; urologist, Belmont Hospital in Worcester; consultant in urology, Fairlawn and St. Vincent's hospitals in Worcester, Harrington Memorial Hospital in Southbridge, and Webster District Hospital in Webster, and consultant in genitoinfectious diseases, Massachusetts Memorial Hospital in Boston; killed Dec. 14, aged 70, by a demented patient.

Spiegel, Leo * New York; born in New York City in 1879; Columbia University College of Physicians and Surgeons, New York, 1901; served as clinical professor of dermatology and syphilology at New York University College of Medicine; specialist certified by the American Board of Dermatology and Syphilology; member of the American Academy of Dermatology and Syphilology; past president of the Yorkville Medical Society; secretary and chairman of the sections on dermatology and syphilology of the Medical Society of the State of New York and the New York Academy of Medicine; on the staffs of Bellevue Hospital and Lenox Hill Hospital, where he died Dec. 17, aged 72, of myocardial infarction.

Kauvar, Solomon Salkind * Denver; University of Chicago, the School of Medicine, 1934; associate clinical professor of medicine at University of Colorado School of Medicine; specialist certified by the American Board of Internal Medicine; certified by the National Board of Medical Examiners; member of the American Trudeau Society; fellow of the American College of Physicians; served as chairman of the Denver Health and Hospital Board; chief division of medicine, Denver General Hospital; attending physician, Colorado General, General Rose Memorial, Mercy, St. Joseph's and National Jewish hospitals; died Dec. 25, aged 41, of astrocytoma of the brain.

Allyn, Gurdon Spicer, Mystic, Conn.; University of Pennsylvania Department of Medicine, Philadelphia, 1903; served overseas during World War I; at one time health officer of New London; on the staff of the Lawrence and Memorial Associated Hospitals in New London; died Dec. 28, aged 72, of heart disease.

Bachmann, Rudolf Friedhold * Fitchburg, Mass.; Cornell University Medical College, New York, 1932; member of the New England Obstetrical and Gynecological Society; fellow of the

American College of Surgeons; certified by the National Board of Medical Examiners; on the staff of Burbank Hospital; died in Evanston, Wyo., Nov. 12, aged 44, in a Union Pacific train accident.

Bailey, Frank Marion, Oklahoma City; Kansas City (Mo.) Medical College, 1901; member of the American Medical Association; served during World War I; formerly medical examiner for the Oklahoma National Life Insurance Company; died Dec. 30, aged 79, of carcinoma of the stomach.

Berkowitz, Joseph Judah, New York; Cornell University Medical College, New York, 1923; served in the Pacific theater during World War II; formerly on the staffs of Flower and Fifth Avenue Hospital, Metropolitan Hospital, and Beth David Hospital; died in Bellevue Hospital Jan. 1, aged 54, of myocardial infarction.

Boal, George Fay, Franklin, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1895; died Jan. 15, aged 80.

Brock, Charles LeRoy * Albuquerque, N. Mex.; George Washington University School of Medicine, Washington, D. C., 1911; died Jan. 5, aged 67.

Brown, George O., Buckhannon, W. Va.; Eclectic Medical Institute, Cincinnati, 1892; died recently, aged 85, of coronary occlusion.

Brown, H. D., Summerville, Ga.; Memphis (Tenn.) Hospital Medical College, 1910; member of the American Medical Association; vice-president of the Farmers and Merchants Bank; died in Riegel Community Hospital, Trion, Jan. 7, aged 66, of coronary thrombosis.

Clark, Guy, Sulphur, Okla.; University of Arkansas School of Medicine, Little Rock, 1908; died Nov. 22, aged 77.

Claytor, John Bunyan, Roanoke, Va.; Leonard Medical School, Raleigh, N. C., 1907; died recently, aged 73, probably of acute coronary occlusion.

Crowley, John Joseph, San Francisco; College of Physicians and Surgeons of San Francisco, 1902; served in the state legislature for many years, first as an assemblyman and later as senator; at one time associated with the epidemiology department of the city health department; formerly superintendent of Mendocino State Hospital in Talmage; died Dec. 30, aged 76.

Davis, Reuben, Philadelphia; Jefferson Medical College of Philadelphia, 1929; member of the American Medical Association; assistant professor of medicine, Temple University School of Medicine; died Dec. 24, aged 47.

DeFreest, Herbert Edwin, Troy, N. Y.; Albany (N. Y.) Medical College, 1893; county welfare physician for many years; served on the staffs of Samaritan and Troy hospitals; died Dec. 25.

Dougherty, Milton Maust, Mechanicsburg, Pa.; Jefferson Medical College of Philadelphia, 1891; died Nov. 22, aged 82.

Elligan, Harry Paul, Detroit; Meharry Medical College, Nashville, Tenn., 1916; died recently, aged 61, of cerebral hemorrhage and essential hypertension.

Emery, Harry Smith * Portland, Maine; born in Buxton, Maine, Jan. 23, 1872; Jefferson Medical College of Philadelphia, 1897; life member of the American College of Physicians; in 1937 president of the Cumberland County Medical Society; in 1947 awarded a 50 year medal by the Maine Medical Association; from 1914 to 1919 instructor in clinical medicine at the Bowdoin Medical School, where he was later assistant professor of medicine; affiliated with Maine General Hospital; died recently, aged 79, of chronic myocarditis and arteriosclerosis.

Engle, Jacob Lenhart, Oxford, Pa.; Medico-Chirurgical College of Philadelphia, 1911; member of the American Medical Association; served during World War I; died Dec. 30, aged 63, of a heart attack.

Fleming, John Clifton, Hartford, Ala.; Medical College of Alabama, Mobile, 1891; died recently, aged 80, of arteriosclerotic heart disease.

Gannone, Peter, Philadelphia; Temple University School of Medicine, Philadelphia, 1925; member of the American Medical Association; on the staff of St. Agnes Hospital; died Dec. 23, aged 51, of coronary thrombosis.

Gardner, Arthur Parcel, Scranton, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1909; served as president of the county school board and the Elmhurst School Board; died in Hahnemann Hospital Dec. 24, aged 68.

Green, Floyd Wesley, Newport News, Va.; Howard University College of Medicine, Washington, D. C., 1929; died Oct. 26, aged 49, of chronic hepatitis.

Harbeck, Edward Vincent, Weaverville, N. C.; North Carolina Medical College, Davidson, 1905; died Oct. 17, aged 86, of arteriosclerotic heart disease.

Hines, Joseph Howard, Atlanta, Ga.; University of Vermont College of Medicine, Burlington, 1900; specialist certified by the American Board of Internal Medicine; formerly on the faculty of Emory University School of Medicine; served overseas during World War I; affiliated with Grady Hospital; on the staff of St. Joseph's Infirmary; died Dec. 3, aged 72, of carcinoma of the bladder.

Hirsch, Edward Klaus, Baton Rouge, La.; Tulane University of Louisiana School of Medicine, New Orleans, 1914; member of the American Medical Association; fellow of the American College of Surgeons; served during World War II; affiliated with Our Lady of the Lake Sanitarium and Baton Rouge General Hospital; died Dec. 26, aged 59, of heart disease.

Hurley, Thomas A., Macon, Ga.; College of Physicians and Surgeons, Baltimore, 1904; member of the American Medical Association; died Dec. 21, aged 72.

Johnston, Joseph Boudinot Jr., Kannapolis, N. C.; Tulane University of Louisiana School of Medicine, New Orleans, 1940; member of the American Medical Association; served during World War II; died in Statesville Dec. 16, aged 37.

Kenney, William, Paris, Ky.; Kentucky School of Medicine, Louisville, 1898; died Dec. 27, aged 74, of a heart attack.

Knight, George Beale, Camden, N. J.; Medico-Chirurgical College of Philadelphia, 1905; died in Gloucester Nov. 26, aged 72, of arteriosclerotic heart disease.

Lanier, Leon Ivey, Soperton, Ga.; Atlanta School of Medicine, 1909; member of the American Medical Association; died Nov. 17, aged 67, of cerebral hemorrhage.

McCarty, Justin Stanislaus Ⓢ Longview, Wash.; University of Oregon Medical School, Portland, 1927; on the staff of Cowlitz General Hospital; died Dec. 27, aged 52, of coronary thrombosis.

McCoy, Benjamin Franklin, Hamilton, Ohio; Medical College of Evansville, Ind., 1878; died Dec. 11, aged 93.

McDaniel, Floyd Cleveland, New York; Medical College of South Carolina, Charleston, 1911; fellow of the American College of Surgeons; died Dec. 31, aged 67.

Mambert, John Wellington Ⓢ Hudson, N. Y.; Albany (N. Y.) Medical College, 1913; served during World War I; on the staff of Columbia Memorial Hospital, where he died Jan. 24, aged 67, of heart disease.

Mangurian, Armen Steven, Manchester, N. H.; Dartmouth Medical School, Hanover, 1907; member of the American Medical Association; on the staff of the Sacred Heart Hospital; died Dec. 15, aged 74, of coronary thrombosis.

Martorell, Abelardo, Tampa, Fla.; Tulane University of Louisiana School of Medicine, New Orleans, 1921; died Dec. 21, aged 54.

Nabers, Samuel Faust, Birmingham, Ala.; Medical Department of Tulane University of Louisiana, New Orleans, 1909; member of the American Medical Association; specialist certified by the American Board of Ophthalmology; on the staff of St. Vincent's Hospital; died Dec. 15, aged 77, of aneurysm of the aorta.

Nelson, Norman Oscar, Orlando, Fla.; Johns Hopkins University School of Medicine, Baltimore, 1904; died Nov. 28, aged 74, of acute coronary occlusion.

Newman, Leon, Boston; College of Physicians and Surgeons, Boston, 1904; died Dec. 27, aged 79, of coronary occlusion.

Oakland, Harry Gustaf Ⓢ Milwaukee; Wisconsin College of Physicians and Surgeons, Milwaukee, 1904; member of the Industrial Medical Association; at one time medical examiner for the fire and police commission; died Dec. 31, aged 73, of coronary arteriosclerosis.

Peavy, Ira Lee Ⓢ Santa Fe, N. Mex.; University of Colorado School of Medicine, Denver, 1924; director of the venereal disease division of the state department of public health; died Dec. 25, aged 62, of cerebral hemorrhage.

Perkins, Harry Bradford Ⓢ Haverhill, Mass.; University of Vermont College of Medicine, Burlington, 1903; fellow of the American College of Surgeons; consulting surgeon, Haverhill Municipal Hospital; died Dec. 19, aged 72.

Potter, William Hale Ⓢ La Mesa, Calif.; University of Buffalo School of Medicine, 1897; an Associate Fellow of the American Medical Association; served overseas during World War I; on the staffs of Mercy and County hospitals in San Diego; died Dec. 28, aged 82, of coronary thrombosis.

Ramer, Paul William, Emmaus, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1926; member of the American Medical Association; for many years on the staff of the Allentown (Pa.) General Hospital; died Dec. 31, aged 50, of malnutrition, secondary to anxiety neurosis.

Reeves, Riley Jefferson, Leicester, N. C.; Vanderbilt University School of Medicine, Nashville, Tenn., 1913; member of the American Medical Association; died Nov. 9, aged 60, of acute congestive heart failure.

Reynolds, Horace Maxwell, Cairo, Ga.; University of Georgia School of Medicine, Augusta, 1943; member of the American Medical Association; served during World War II; drowned in Tallahassee, Fla., Nov. 19, aged 33, in a motorboat accident.

Roberts, Lily, Fort Worth, Texas; Physio-Medical College of Texas, Dallas, 1908; member of the American Medical Association; died Nov. 5, aged 75, of cerebral hemorrhage.

Scott, Walter, Headland, Ala.; Atlanta School of Medicine, 1910; died recently, aged 65, of pulmonary tuberculosis.

Spence, George Segars, Vineland, N. J.; Jefferson Medical College of Philadelphia, 1905; died Nov. 30, aged 60, of pulmonary emphysema.

Taylor, John Francis, Mobile, Ala.; Meharry Medical College, Nashville, Tenn., 1916; died recently, aged 62, of cerebral hemorrhage.

Tidd, Charles Henry, Whittier, Calif.; University of Pennsylvania School of Medicine, Philadelphia, 1912; died Nov. 2, aged 62, of bronchiectasis and congestive heart failure.

Timberlake, Claude Vernon, Youngsville, N. C.; Jefferson Medical College of Philadelphia, 1915; died Nov. 16, aged 60, of coronary occlusion.

Vandiver, Horace Greely, Trenton, Ala.; Vanderbilt University School of Medicine, Nashville, Tenn., 1915; died in Huntsville Nov. 8, aged 70, of coronary occlusion.

DIED WHILE IN MILITARY SERVICE

Martin, Gerald Arthur Ⓢ lieutenant, U. S. Navy, Towson, Md.; Medical College of Virginia, Richmond, 1946; served an internship and residency at University Hospital in Baltimore; in July, 1947, began active duty as a lieutenant (jg) in the medical corps of the U. S. Naval Reserve; later transferred to the regular navy; died in Isehara, Japan, Sept. 27, aged 28, of injuries received in an airplane accident.

GOVERNMENT SERVICES

PUBLIC HEALTH SERVICE

Dr. Mider Becomes Scientific Director.—Dr. G. Burroughs Mider, professor of cancer research at the School of Medicine and Dentistry at the University of Rochester, New York, has been appointed scientific director at the National Cancer Institute of the National Institutes of Health. Dr. Mider will be responsible for the intramural research of the National Cancer Institute. In 1938 he was appointed a National Cancer Institute research fellow and assigned to the University of Rochester under Dr. John J. Morton.

Dr. Mider and Dr. Morton were among the first cancer research workers to produce skin cancer in laboratory animals with a single application of a chemical of known composition, the first to produce leukemia in experimental animals under controlled conditions, and the first to show that solvents of a cancer-causing agent might also inhibit the ability of that agent to cause cancer.

Dr. Mider in 1941 became instructor in pathology at the Medical College of Cornell University. He was made assistant professor the next year and remained at Cornell until 1944, when he joined the faculty of the Medical School of the University of Virginia as associate professor of pathology. Since 1945 he has been on the faculty of the School of Medicine and Dentistry at the University of Rochester, first as research associate, and since 1948 as professor of cancer research and coordinator of cancer teaching. He is also a consultant to the Rochester Laboratories of the Atomic Energy Commission. He became a diplomate of the American Board of Pathology in 1945.

Laboratory Training Courses.—The following schedules of laboratory training courses for 1952 have been announced by the Communicable Disease Center:

Bacterial diseases: part 1, general bacteriology, Sept. 2-12; part 2, general bacteriology, Sept. 15-26.
 Enteric diseases: enteric bacteriology, Sept. 20 to Oct. 10.
 Microbiology for public health nurses, May 19-23.
 Mycology: part 2, systemic fungi, April 14-25.
 Parasitic diseases: part 1, intestinal parasites, Sept. 2-26; part a, blood parasites, Sept. 29 to Oct. 17.
 Pulmonary mycoses, Nov. 24 to Dec. 12.
 Rabies, April 7-11 and Dec. 1-5.
 Syphilis: serology, April 14-25, May 12-23, Sept. 8-19, and Oct. 13-24; preparation and use of controls in serologic tests, Nov. 3-21.
 Tuberculosis, April 14-25, and Nov. 10-21.
 Venereal diseases, May 12-16.
 Virus diseases, Nov. 10-21.

Courses in laboratory diagnosis designed for laboratory directors, senior laboratory staff members, physicians, and others of comparable professional standings are as follows:

Bacterial diseases, May 12-16, and Oct. 27-31.
 Parasitic diseases, May 12-16, and Nov. 10-14.
 Tuberculosis, May 19-23, and Nov. 3-7.
 Venereal diseases, May 12-16.
 Virus diseases, May 12-16, and Nov. 24-28.
 Medical mycology: laboratory methods, Nov. 17-21.
 Treponema pallidum: immobilization test, May 19-23.

Information should be requested from the Laboratory Training Services, Communicable Disease Center, Public Health Service, P. O. Box 185, Chamblee, Ga.

Last Year's Record in Live Births.—In the United States last year the live births exceeded 3,800,000 for the second time in history, according to vital statistics released March 6 by the Public Health Service. The 1951 total may be an all-time high for the United States, the service said. The number of children born in 1951 was estimated at 3,833,000 as compared with the 3,818,000 born in 1947, the previous record year. The annual birth rate for 1951, based on registered births alone, rose to 24.5 per thousand population, an increase of 4.3% over 1950.

The infant mortality rate, which dropped for the 15th straight year, helped to swell the 1951 addition to the infant population.

Infant deaths last year occurred at the rate of 28.8 per thousand live births, contrasted with a rate of 47.4 in 1940 and 64.8 in 1930. The over-all death rate, 9.7 per thousand population, showed virtually no change from 1950. The mortality level has now been below 10 deaths per thousand population for four years in a row.

Examination for Sanitary Engineers.—Competitive examinations for the appointment of officers as sanitary engineers in the regular corps of the United States Public Health Service will be held on June 3-5 at a number of points throughout the United States. Applications must be received no later than April 30, 1952. A regular corps appointment is permanent in nature and provides an opportunity for a qualified engineer to make a life career in engineering as it relates to the protection and promotion of public health.

Application forms may be obtained by writing to the Surgeon General, Public Health Service, Federal Security Agency, Washington 25, D. C., Attention: Division of Commissioned Officers.

VETERANS ADMINISTRATION

Korean Veterans.—The Veterans Administration announced March 10 the number of military personnel who have returned to civilian life as veterans since the Korean conflict started June 27, 1950. By January, 1952, there were 655,000 living veterans who had had U. S. military service since the Korean conflict began. This is an average discharge rate of nearly 35,000 a month for the 19 month period. As of Dec. 31, 1951, a total of 3,988 were drawing compensation for service-connected disabilities or pension for nonservice-connected disabilities.

VA hospitalization was being provided on Jan. 31, 1952, for 1,862 veterans with service since Korea. In addition to living veterans with service since Korea, the VA was furnishing benefits to dependents of deceased veterans of the Korean conflict. As of Dec. 31, 1951, 17,061 dependents of 8,895 such deceased veterans were receiving VA death compensation or pension. On the same date, VA had allowed 4,521 claims for indemnity payments to survivors under Public Law 23, the Servicemen's Indemnity and Insurance Acts of 1951. This is the law that provides a free indemnity of up to \$10,000 less any GI insurance in force for the immediate family of eligible servicemen and women who die in service or within 120 days of their discharge from service.

Vacancies for Residents.—The Crile Veterans Administration Hospital of Cleveland announces that there are several vacancies for residents in internal medicine, psychiatry, neurology, and otolaryngology beginning July 1, 1952. Physicians interested should apply to Dr. Joseph T. Wearn, Chairman, Dean's Committee, Western Reserve University School of Medicine, 2065 Adelbert Rd., Cleveland 6, Ohio, or to Dr. Leon Ross, Chief, Professional Services, Veterans Administration Hospital, 7300 York Rd., Cleveland 29, Ohio.

Personal.—Isaac D. Welt, Ph.D., has been appointed assistant director and principal scientist of the Radioisotope Unit, Veterans Administration Hospital, Houston, Texas, and assistant professor of biochemistry at Baylor University College of Medicine. Dr. Welt was formerly on the staff of the division of nutrition and physiology of the Public Health Research Institute of the City of New York, Inc.

Staff Psychiatrist Wanted.—There is an opening for a staff psychiatrist at the Veterans Administration Hospital, Hines, Ill. This hospital is located on the western outskirts of metropolitan Chicago. Certification or Board-eligibility is required. The salary range is from \$5,500 to \$9,600, plus 25% for certification.

FOREIGN LETTERS

FINLAND

Lumbar Sympathectomy for Arterial Disease.—Professor Hämäläinen, who is in charge of the Kuopio County Hospital, has for years been interested in the treatment of obliterative disease of the arteries of the legs by lumbar sympathectomy or gangliectomy. One of his assistants, Dr. T. Gunnar Nyström, recently made a systematic investigation of the results achieved by this operation in 143 patients thus treated from 1937 to 1943. Results of this study have been published in a 127-page supplement to *Acta Chirurgica Scandinavica*. Among the 143 patients, 106 were found suitable for critical analysis of their condition since the operation. The 143 patients were classified into four groups according to age on admission to the hospital. There were 24 patients in group 1 (under age 40), 46 in group 2 (ages 10 to 49), 48 in group 3 (ages 50 to 59), and 25 in group 4 (over age 60). This simple classification was preferred, because of the comparatively difficult task of distinguishing by clinical standards between the various forms of arterial disease for which this treatment is considered suitable.

The 106 patients analyzed were classified according to their present condition: 37 showed improvement, 27 showed no sign of progress of the disease since the operation, 19 showed deterioration, and 23 required a major amputation. Broadly speaking, about three-fifths of these patients had benefited from the operation or showed no progress of the disease after it. The patients in age groups 2 and 3 showed, on the whole, better results than patients in the youngest and oldest age groups. The duration of the disease before the operation apparently had no influence on the postoperative prognosis. The operation was followed, in many cases, by cessation or mitigation of spontaneous attacks of pain, but intermittent claudication was rarely banished completely, although it may have been diminished in some cases. The disease seemed to be more amenable to operative treatment when it was associated with other symptoms than when it dominated the clinical picture as a more or less isolated phenomenon. Of 28 patients who had open sores (usually small) at the time of the operation, there were ten whose sores had healed at the time of the follow-up examination. The various ischemic disturbances had improved in about one-half of the patients. In 21.5% of the patients amputations could not be avoided, in spite of the sympathectomy; 15 of the patients requiring amputation had open sores on the legs before the original operation, and five had had severe attacks of spontaneous pain. Some physicians believe that lumbar gangliectomy may delay the necessity for amputation for several years, but Dr. Nyström found that more than one-fifth of these patients had to undergo an amputation, which, in most cases, took place within a year of the operation. In view of the varied postoperative careers of these patients, Dr. Nyström states that he has experienced considerable difficulty in determining the general rules to be followed in selecting cases suitable for this treatment.

Tapeworm Problems.—The tapeworm (*Diphyllobothrium latum*) is such a common parasite in Finland that, according to some authorities, about 20% of the people harbor it. There are some areas in Eastern Finland in which every inhabitant is or has been at some time its host. According to Dr. Osmo Vartiainen of Helsingfors, the frequency of its occurrence in humans in this country is a result of the prevalence of fish in the people's diet. Inadequate cooking and salting of fish that come from the many inland waters, as well as mass migrations due to war conditions, favor the continued prevalence of this parasite. Yet most of the people fail to take the necessary precautions, which are particularly apt to be neglected when frozen fish obtained from areas in which the worm is endemic are used.

This worm may not cause harm comparable to that caused by tuberculosis and rheumatism, but it is a nuisance. Its host may have recurrent attacks of diarrhea as well as general

malaise, giddiness, emaciation, and lassitude; however, as a rule the host's reaction is so slight that he is unaware of the worm's presence until he finds it by chance in his feces or until it is discovered when he is examined for some other ailment. The frequency with which this worm causes pernicious anemia was probably underrated in the past. It is difficult to estimate the degree of invalidism and economic loss this worm inflicts on the community, but it has been calculated that over 100,000 treatments with extract of male fern (*Aspidium* [*Dryopteris*] *filixmas*) are undertaken each year at a loss of at least one day's work for each treatment. In addition, working capacity is impaired, because of the debilitating effects of the worm. In view of these national economic losses, there is a need for an educational campaign and for provision of a satisfactory anthelmintic. Extract of male fern has held its place in this field for decades, but it is by no means an ideal remedy, partly because of the difficulty of exactly standardizing its most potent constituent elements. It has been responsible for several deaths as well as for blindness. It is sold without a physician's prescription and is often taken in haphazard fashion by patients who may not even harbor the worm and who are apt to neglect the important precaution of following this remedy with a purgative or an enema. They may also make the mistake of combining an anthelmintic with alcohol, which promotes its absorption by the host.

The Late Professor Suolahti.—Prof. Eino Suolahti, the distinguished Finnish surgeon, died in 1951 from cerebral thrombosis. He was born on Nov. 7, 1879, with a family history in the best Finnish tradition. The son of a schoolmaster, he began his academic career as a chemist but soon switched to medicine. He qualified as a physician in 1909 and took his doctorate in 1926, with a study of the development of certain parts of the larynx. He practiced as an otolaryngologist in Helsingfors for many years and served as chairman of the medical society Duodecim and of the Finnish Medical Association. His gift for administration became well known and appreciated during his association with the hospital services in Helsingfors. When a crisis arose in the Finnish army medical service during the fighting between Finland and the U.S.S.R. in December, 1939, Field Marshal Mannerheim called on him to take charge of this service. During the campaigns of 1939 and 1944, he did much to assure the smooth operation of this service. Suolahti combined a passionate devotion to the culture and political ambitions of his country with a gift for meeting his fellow beings with even-tempered suavity.

ITALY

Iron Metabolism in Patients with Jaundice.—Drs. Ferri and Scavo discussed iron balance in patients with hepatocellular type of catarrhal jaundice caused by angiocholitis and stasis, at a meeting of the Medicosurgical Society of Pisa, held under the chairmanship of Professor Massart.

In all the patients observed, iron metabolism was studied before and after oral and parenteral administration of iron. Metabolic deviations were observed only in patients with hepatocellular jaundice and with jaundice from stasis associated with a tumor of the head of the pancreas. There was a pronounced increase in the blood iron level, a decrease in absorption, and a normal excretion of iron, especially in patients with catarrhal jaundice of hepatocellular type. After oral administration of iron, the increase in the blood iron level was slight, and retention of the ingested metal was also slight; after intravenous administration, the iron quickly disappeared from the circulation.

In patients with jaundice resulting from an obstruction of the common bile duct, caused by tumors of the head of the pancreas, the blood iron level was normal or low, and absorption was diminished. After oral administration of iron, the blood

iron level increased only slightly, and the ingested metal was almost completely excreted.

On the contrary, iron metabolism was almost normal in patients with jaundice caused by angiocholitis and lithiasis; in these patients, there were no evident functional alterations of the hepatic cell; otherwise, anomalies, similar to those seen in patients with catarrhal jaundice of hepatocellular type, were observed.

The speakers concluded that diminution of the biliary flow does not cause changes in iron metabolism. In patients with catarrhal jaundice of the hepatocellular type, the high blood iron level may be attributed to faulty storage of the metal in the liver, because of the lesion of the hepatic cell; although excretion is carried out in the normal way, the high blood iron level arrests iron absorption at the level of the intestine. In patients with jaundice resulting from stasis from neoplasms of the pancreas, the tendency to a low blood iron level and the poor retention of the ingested iron may be attributed to disturbances of digestion and absorption caused by the decreased biliary and pancreatic flow that are characteristic of pancreatic lesions.

Society of Anesthesiology.—The southern section of the Italian Society of Anesthetists held a meeting in Naples under the chairmanship of Prof. Ettore Ruggieri. Drs. A. Ruggiero and F. Lezza reported on intravenous administration of procaine hydrochloride. They discussed toxic reactions, emphasizing that even the severest complications are not fatal if treated in time. Numerous tests to prove sensitivity to procaine hydrochloride have been proposed; on the basis of Richard's experiments, simultaneous administration of vitamin C in adequate doses diminishes the incidence of convulsive complications and increases tolerance to procaine.

In discussing the use of procaine in anesthesiology and in postoperative treatment, the speakers, on the basis of the literature and of their personal experience, classified intravenous procaine in the following way: (1) an adjuvant to anesthesia, (2) the only anesthetic agent, (3) an agent preventing and treating cardiovascular alterations that may occur during anesthesia and during operations on the thoracic cavities, (4) an agent preventing and treating some forms of peripheral vascular insufficiency, and (5) an analgesic agent for the postoperative period. The largest doses used by various authors, as reported in the literature, are 20 gm. in eight hours (Edmonds), 21 gm. in four hours (Bittrich), and 25 gm. in seven hours (Moreno). The largest dose administered by the speakers was 11 gm. in three and one-half hours. The largest total dose administered to the same patient before, during, and after operation was 29 gm. The speakers' clinical material includes information on the administration of procaine in anesthesia to 93 patients who had operations on the neck, thorax, abdomen, and extremities and to 211 patients for postoperative treatment. They concluded that intravenous procaine used according to appropriate instructions, doses, and techniques may give gratifying results and suggested a wider adoption of the intravenous use of this drug.

During the discussion period, Dr. Bracale pointed out the advantages that the intravenous administration of procaine hydrochloride has over surface analgesia of the tracheobronchial tree for tracheal intubation and bronchial exclusion, because it causes areflexia of the respiratory tracts.

On the basis of his personal experience, Dr. Bracale expressed the opinion that intravenous procaine, as an adjuvant to any type of anesthesia, represents considerable progress and does not cause inconvenience or harm. Dr. Aghina, on the basis of his experience in French hospitals, asserted the utility and the advantages of anesthesia by intravenous administration of procaine hydrochloride; however, his method differs from that of the speakers. It consists in the infusion of a 1:1,000 solution of procaine hydrochloride in a glucose solution combined with 0.50 gm. of thiopental (pentothal®) sodium for each gram of procaine given to the patient in his room 30 minutes before the operation. Anesthesia is completed with small doses of thiopental sodium, nitrogen protoxide, and curare-like substances. In this way, intubation is made easier. The total dose administered by Dr. Aghina is less than that of Drs. Ruggiero and Lezza. The speaker mentioned the contraindications for simultaneous administration of physostigmine salicylate (eserine) and neostigmine.

LONDON

Charges for Parts of Health Service.—The recently elected conservative government has decided to make charges for various parts of the health service. These charges are designed to avoid abuse of the facilities of the service. In this time of financial crisis, the vast cost of the health service is a threat to the solvency of the country. Since the introduction of the service, there has been a steady increase in the number of prescriptions written from about 202,000,000 in 1948 to 229,000,000 at present. This has cost the taxpayers about \$140,000,000 a year. There is little doubt that some patients, in the past, have made inordinate demands on the national medicine chest; for instance, there has been an increase in the use of such things as cotton wool. There is, however, a potential willingness on the part of physicians to encourage their patients to use less medicine. Prof. D. M. Dunlop, who, with several colleagues, has analyzed the contents of about 17,000 prescriptions written on the National Health Form E.C.10., thinks that physicians should be given the chance to educate their patients away from the "bottle of medicine" habit. One objection to the charges is that the money is to be collected by the physician himself, thus adding to the numerous petty nonmedical tasks with which the family physician has to cope, and, if he neglects this new obligation to the Ministry of Health, he is likely to lose money, because an amount will be deducted from his salary equivalent to the amount he should have collected for the prescriptions he issued.

War pensioners are exempt from the charges, but persons with long and chronic illnesses have to pay for their prescriptions, even though it is not the genuinely chronically ill who are responsible for nonessential prescribing. The scheme of charges will require such persons as old age pensioners to pay a charge for their medicine or undergo a means test before receiving national assistance. The *British Medical Journal* calls for a clearer statement of policy on the part of the new conservative government. It has been computed that during the past year, there was an expenditure by Britons of \$2,178,000,000 (£778,000,000) on tobacco, \$1,366,000,000 (£488,000,000) on beer, \$1,280,000,000 (£650,000,000) on gambling, and \$299,000,000 (£107,000,000) on the cinema. One would think that token charges for medical services could well be borne by the British public. Token charges cannot, by any stretch of imagination, create a financial barrier to treatment; however, the old age pensioners and the debilitated, chronic sufferer, who is to have frequent medicaments and faces a long illness might require special consideration. So should the family physicians who are supposed to collect the charges. Surely, there are enough lay clerks in hospitals and attached to the Ministry of Health to cope with this new drudgery; however, perhaps any step is a good one if it quells the attitude of the welfare state, that is, "something for nothing." A government that molluscates the citizen saps his initiative and his sense of responsibility and may bring his health into a parlous state.

Survey of Prescriptions for Drugs.—Prof. D. M. Dunlop, F.R.C.P., and two colleagues have reviewed by statistical analysis of 17,301 prescriptions the relative frequency with which different drugs are prescribed. Material was collected from the department of therapeutics of the University of Edinburgh. The materials used were the prescriptions issued on form E.C.10 of the National Health Service during September, 1949. They were anonymous, as the name of the prescribing practitioner had been deleted. Although the authors of the survey did not know how many family physicians took part, they thought the number to be about 140. Prescriptions came from a cross section of the community, the areas from which they were derived being classified as the prosperous residential, the industrial, and the mixed suburban types. Districts of each type included several of dissimilar geographic and administrative distribution. For instance, districts of the industrial type were taken from the north, from the midlands, and from the west of England. The first problem considered was whether the drugs prescribed were proprietary or nonproprietary. It was found that approximately 21% of prescriptions written were for proprietary drugs. There was reason to believe that this percentage had risen in the past year. Mixtures and tablets accounted for 68% of all prescriptions; drugs and appliances accounted for 9%, whereas injections for only 1.5% of the total. This suggested that this

method of administering drugs, which was so popular in Continental Europe, was not a feature of English medical practice. Another 1.5% of the total prescriptions was devoted to powders. Stomach powders, in particular, gave place to more expensive and cumbersome mixtures.

As for the actual drugs, or groups of drugs, it was found, and the authors regard it as a significant commentary on present day conditions, that hypnotics and sedatives formed the largest group, being 15% of all the drugs prescribed. This 15% was made up of 9.4% barbiturates and 5.8% bromides. Chloral hydrate was only occasionally incorporated in the bromide mixture. The authors thought it strange that this hypnotic should so seldom find its way into the prescriptions. Those prescriptions that came under the heading of tonics were found to include many "elegant and complex recipes." They seemed little more than placebos of doubtful value. Expectorant cough mixtures came under criticism because they contained a large proportion of sedative and the expectorant was often of an inadequate dosage and of doubtful effect, even if given in sufficient amounts. About 40% of the vitamin prescriptions were of a proprietary nature. The authors deplored this, as they were of the opinion that prescription of vitamins was unnecessary in England, whose food supply, although meager, is cheap, and, if care is taken in the choosing and cooking of the food, there should be no avitaminosis. There is, perhaps, some justification for the prescription of ascorbic acid during the winter months.

Penicillin formed about 4% of the total prescriptions, 6.9% of these consisting of parenteral injections; however, 30% of the penicillin prescriptions were for oral preparations and more than 40% for penicillin ointments. This may be accounted for by the fact that many injections may have been given from the family physician's own stock. A remarkably small number of prescriptions for epinephrine appeared, in view of the fact that asthma is such a common condition. Iron, on the whole, was prescribed according to British Pharmacopoeia standards. Iron and strychnine mixtures were generally classified as tonics. There was a curiously low number of prescriptions for laxatives, suggesting that many persons still buy their laxatives from druggists. Another curious anomaly was that liver preparations were ordered 118 times in comparison with 68 prescriptions for insulin, suggesting that liver was often prescribed as a general tonic or as an antianemia therapy in patients other than those suffering from anemia that required a hemopoietic factor. This is indeed strange, as diabetes is a common disease, and megaloblastic anemias are comparatively rare. The increased popularity of amphetamine is brought out in this survey, the drug being prescribed 218 times. Diacetylmorphine (heroin) made up about one-third of prescriptions for the stronger analgesics. Among the more rarely prescribed drugs was mersalyl, which was prescribed fewer than 20 times, but it may have been often prescribed from a family physician's own stores. Such multiple preparations as a combination of iron, folic acid, and liver or hog's stomach, which are unjustifiable on therapeutic grounds, were only rarely prescribed. Another interesting factor was the prescription of thiouracil, which was prescribed only twice in 17,301 prescriptions. This is contrary to expectations, as the family physician often writes a prescription for maintenance treatment, the original treatment being carried out under hospital supervision. The conclusion drawn from this is that the conservative treatment of thyrotoxicosis is surprisingly uncommon in England.

Professor Dunlop concludes his review by saying that its object was to show important trends in prescribing in an objective and uncontroversial manner. He thought it possible that good prescribing is often economical prescribing, and he was of the opinion that the writing of prescriptions should, if possible, be brought into line with the country's financial difficulties. He also thought that the practice of teaching pharmacology in the preclinical years could probably be reviewed with some benefit and improvement made in the therapeutic knowledge of recently qualified physicians.

Parrots Reprieved.—The Ministry of Health has announced the lifting of the ban imposed 21 years ago on the importation of parrots, budgerigars, and cockatoos. The following reasons are given for this step. 1. There has been no significant outbreak of psittacosis in this country since the ban was imposed. 2. It

is now known that psittacosis occurs in other birds, such as seagulls, ducks, and turkeys. 3. The disease is efficiently controlled by the antibiotics. Only one death from psittacosis has occurred in England and Wales during the last 10 years. It is pointed out that the lifting of the ban does not affect other legal requirements, e. g., the need for obtaining a Board of Trade license to import a seed eating bird.

NORWAY

ACTH from Whales.—Chemical manufacturers Nyegaard & Co. (Nyco) have for some time taken an active interest in the exploitation of the hypophyses of whales as a source of corticotropin (ACTH). Late in 1951, Dr. Evang, who is head of the Norwegian Ministry of Health, announced that Nyco and the whaling companies had made a gift of 25,000 bottles of corticotropin for use in Norwegian hospitals where clinical research is being carried out in this field. During the last whaling season, some 9,000 whale hypophyses, weighing about 185 kg., were collected and dealt with as a source of corticotropin. At the rates at the end of 1951, the value of this gift may be put at approximately 400,000 kroner. The 25,000 bottles contain a quantity of corticotropin corresponding to 625,000 I. U. The distribution of this gift among different hospitals is being carried out so as to assure its employment by research workers qualified to make the best use of it.

In a recent issue of *Nordisk medicin*, Dr. Jakob Valsö gave an account of the methods he has employed in removing hypophyses from whales from the Antarctic. He pointed out that the hypophysis of the blue whale has an average weight of 34.6 gm., the anterior lobe weighing as much as 32.5 gm., while the posterior lobe weighs only 1.4 gm. and the pars tuberalis only 0.7 gm. He secured the anterior lobe by thrusting his hand through the foramen magnum after the hypophysis had been loosened from its surroundings by cutting a ring with a knife against his index finger. Working in this way, in the dark, he usually damaged the posterior lobe whose connection with the anterior lobe he found to be quite loose. This looseness of the connection facilitates the separation of the two lobes and examination and exploitation of each lobe by itself. He has come to the conclusion that gonadotropic hormones are to be found in the anterior lobe in approximately the same quantities as in the corresponding gland in cattle. The thyrotrophic hormone is to be found in quantities greater than those extracted from the hypophyses of cattle but less than those from the hypophyses of pigs. Considering how small the posterior lobe is in comparison with the anterior lobe in the blue whale, and how minute the former is compared with the total weight of this whale, Dr. Valsö expressed surprise over its ability to produce sufficient quantities of posterior lobe hormones. He hopes that it may be possible to prepare a whole extract of the anterior lobe suitable for injection.

Three New Cases of Leprosy in Norway.—Until recently, there were only 11 known patients with leprosy in Norway, all of them segregated in a leper hospital headed by Dr. Reidar Melsom in Bergen. With a population of three million persons, this leprosy rate is lower than that of the United States and many European countries; however, in 1951, three new cases of leprosy were discovered. The three patients belonged to the same family, two brothers and one sister. There had been leprosy in their family before, two maternal grandmothers and the mother having suffered from it. The mother was admitted to the leper hospital in 1931, suffering from advanced tuberculous leprosy. She died in 1933. It would, therefore, seem that the last occasion on which her children could have been infected was a score of years ago, an interval indicative of the long incubation period and chronic course of the disease.

Giving details of these three cases in the organ of the Norwegian Medical Association, *Tidsskrift for den norske lægeforening*, for Feb. 1, Dr. Melsom points out how easy it is to overlook the true character of the disease when the possibility of it is not kept in mind and the physician concerned does not have the family history before him. Yet this possibility is by no means negligible, since Norway has the third largest merchant fleet in

the world and her seamen are at times exposed to massive infection in the tropics. Since 1930, there have been three cases of leprosy discovered in seamen returning from abroad.

The three patients whose disease was discovered in 1951, were born in 1913, 1923, and 1925, respectively. It was only after the disease had been recognized in the two youngest patients that a search was made for it in their nearest relatives, including their elder brother, who was at sea when they were found to be lepers. Dr. Melsom contacted this seaman's ship's physician who consulted several specialists in leprosy who were with him. None of these specialists was sure whether the sailor was a leper. On examination in Bergen, this patient had a papular eruption on the trunk and limbs and numerous nodules, both cutaneous and subcutaneous, varying in size from that of a pinhead to that of a pea. A biopsy showed a typical leproma. The youngest patient also presented diagnostic problems, for, in 1940, when he had consulted a neurologist for wasting of his hands, the diagnosis was a lesion of the peripheral nervous system, and the treatment given was electrical. It was not till the summer of 1950, that his rash began to appear, and, at first, little attention was paid to it. In all three patients, involvement of the peripheral nerves led to the correct diagnosis.

Treatment of Cancer of Uterus.—Since May, 1932, treatment of cancer of the cervix has been almost completely centralized in the Norwegian Radium Hospital just outside Oslo. On the other hand, patients with cancer of the body of the uterus have, to a large extent, been distributed through various hospitals, in which they have received surgical treatment. As recently pointed out by Dr. Ragnvald Bredland, who is on the staff of the Norwegian Radium Hospital, for some time there has been a growing tendency for these patients also to be admitted to the Radium Hospital. This tendency reflects the growing appreciation of radiotherapy for corpus as well as cervix cancer. Between 1932 and 1949, the number of patients with corpus cancer treated every year at this hospital has been trebled. Dr. E. Schjött-Rivers, who is in charge of the gynecologic department of the Radium Hospital, has adopted a discriminating attitude toward the treatment of corpus cancer cases, giving radiologic treatment alone in some instances, radiologic treatment followed by operative treatment in others, or postoperative radiologic treatment.

Dr. Bredland has published in *Nordisk medicin*, Dec. 5, certain calculations showing, among other things, what the chance is of discovering corpus or cervix cancer by the wholesale examination of women in various cancer predisposed age groups. For example, he calculates that between the ages of 45 and 60, some 2,000 women will have to be examined for every new case of cancer discovered. Another of his calculations concerns the relative frequency of corpus and cervix cancer. In the older textbooks, it was assumed that for every case of corpus cancer there were from 5 to 10 cases of cervix cancer; but now that patients with both types of cancer of the uterus are being centralized in one hospital, the comparative corpus-cervix rate is approximately one to three, as it is in Denmark.

Expansion of the Norwegian Radium Hospital.—Dr. Reidar Eker, who is head of the Norwegian Radium Hospital, in which cancer patients from all parts of the country are centered, pointed out that by the end of 1951, the public had contributed more than 15 million kroner to the enlargement of the hospital. The main wing of the new building will hold 150 hospital beds. There will also be a hostel with 40 beds for patients as well as accommodations for nurses and other members of the staff. In the plans for this expansion, it was calculated that the cost would come to 14.7 million kroner, but, during the last two years, the cost has risen by 20%, and there is no guarantee that this upward movement will not continue. The public is therefore being urged to contribute still more this year, and the government is encouraging such contributions by exempting them from taxation. A notice to this effect is printed in the income tax forms issued to taxpayers. Even if gifts by the public cover more than the cost of this expansion, there will be ample opportunities for investing them for the benefit of cancer patients for whom hospital accommodation is required in Bergen and Trondheim also. Besides, there is no limit to the financial requirements for cancer research.

CORRESPONDENCE

CONGENITAL ANOMALIES AND CORTISONE

To the Editor:—The experimental production of congenital anomalies with cortisone reported in an editorial in *THE JOURNAL* (148:206 [Jan. 19] 1952) furnishes an additional clue to the possible role of cortical hypoadrenia in these defects.

It is well established that following administration of large doses of cortisone a temporary cortical hypoadrenia develops. Normal physical and cerebral development in utero seems to be dependent upon an intact adrenal cortex (Pappenheimer, Sajous).

I suggested in 1947 that injury to the embryonic adrenal cortex by the virus of rubella during a short critical period early in pregnancy was the cause of subsequent congenital defects (Cause of Congenital Defects Following Rubella in Mother: Role of Adrenals, *Northwest Med.* 46:288 [April] 1947).

Regarding defects induced in the offspring of cortisone-treated pregnant mice, Fraser and Fainstat (*Pediatrics* 8:527 [Oct.] 1951) state: "In general, the earlier treatment was started the more severe were the defects observed." This suggests that suppression of embryonic cortical secretion, resulting from large doses of cortisone given in early pregnancy, may account for the subsequent maldevelopment of the embryo.

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FACTOR 5 DEFICIENCY IN HEMORRHAGIC DIATHESIS

To the Editor:—I was very much interested in the paper entitled "Factor 5 Deficiency in Hemorrhagic Diathesis (Parahemophilia)" by Stuart W. Cosgriff and Edgar Leifer which appeared in *THE JOURNAL* (148:462 [Feb. 9] 1952). There is little doubt that this patient actually had a deficiency of factor 5 associated with a mild prothrombin deficiency and fibrinopenia. Our interest in this case report, however, comes from the fact that we have recently published a study of the hemorrhagic diathesis occasionally seen in patients with cancer of the prostate, metastatic to bones. In this small series of patients (H. J. Tagnon, W. Whitmore, and N. R. Shulman: Fibrinolysis in Metastatic Cancer of the Prostate, *Cancer*, 5:9, 1952), we observed for the first time the presence of marked fibrinolysis in the blood. We could demonstrate the presence of a proteolytic enzyme in the blood of these patients, which was able to digest fibrinogen and ac-globulin. The result was, in these patients, the production of a hemorrhagic diathesis. It was interesting to observe that the periods during which bleeding was present coincided with the presence of fibrinolysis in the blood. Further details on these cases are available in the above-mentioned paper. Our interpretation of fibrinolysis in patients with metastatic cancer of the prostate is that the proteolytic enzyme normally present in prostatic tissue gains access to the circulating blood and can be occasionally detected in the blood of these patients if a search is made for fibrinolysis. My impression is that the deficiency of factor 5 found in the case reported by Drs. Cosgriff and Leifer could be explained on the basis of the presence of fibrinolysis in the blood of this patient. No search for fibrinolysis was made by these authors, and my impression is further confirmed by the fact that associated with the factor 5 deficiency there was also a deficiency of fibrinogen and prothrombin in this case, in contrast to the case reported by Owren, in which the deficiency of factor 5 was not associated with a deficiency of the other coagulation factors. If this interpretation is correct, the case reported by Drs. Cosgriff and Leifer would constitute another instance of this new syndrome first described by us.

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COUNCIL ON MEDICAL
EDUCATION AND HOSPITALS

INTERNSHIPS AND RESIDENCIES

The following internship and residency training programs were approved by the Council on Medical Education and Hospitals of the American Medical Association at its meeting in Chicago, Feb. 9, 1952. A number of hospitals not included in this list have been surveyed by representatives of the Council and have been recommended for internship and/or residency approval. These hospitals will be notified as soon as final action on their applications has been completed.

Additional information regarding the hospitals listed below will appear in the next Internship and Residency Number of THE JOURNAL, scheduled for publication on Sept. 27, 1952.

ADDITIONAL INTERNSHIPS APPROVED

Veterans Administration Hospital.....	Dearborn, Mich.
Veterans Administration Hospital.....	Seattle, Wash.
Weld County Public Hospital.....	Greeley, Colo.
Manchester Memorial Hospital.....	Manchester, Conn.
Presbyterian Hospital.....	Newark, N. J.
St. Joseph Hospital.....	Hazleton, Pa.
Chester County Hospital.....	West Chester, Pa.
Providence Hospital.....	Waco, Texas
Memorial Hospital.....	Danville, Va.
Kudlee Hospital.....	Richland, Wash.

ADDITIONAL RESIDENCIES APPROVED

Anesthesiology

Kansas City General Hospital, No. 1.....	Kansas City, Mo.
Queens General Hospital.....	Jamaica, N. Y.
Allentown Hospital.....	Allentown, Pa.

General Practice

St. Mary's Hospital.....	Tucson, Ariz.
Glockner-Pearse Hospital.....	Colorado Springs, Colo.
Wilmington General Hospital.....	Wilmington, Del.
South Shore Hospital.....	Chicago, Ill.
Lutheran Deaconess Hospital.....	Minneapolis, Minn.
St. Mary's Memorial Hospital.....	Knoxville, Tenn.
Baptist Hospital.....	San Antonio, Texas
Kudlee Hospital.....	Richland, Wash.
Maynard Hospital.....	Seattle, Wash.
Sacred Heart Hospital.....	Spokane, Wash.
Bluefield Sanitarium.....	Bluefield, W. Va.

Internal Medicine

Veterans Administration Hospital.....	Omaha, Neb.
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Ophthalmology

Parkland Hospital.....	Dallas, Texas
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Pediatrics

St. Joseph Hospital.....	Syracuse, N. Y.
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Plastic Surgery

Beth Israel Hospital.....	New York City
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Psychiatry

U. S. Naval Hospital.....	St. Albans, N. Y.
Veterans Administration Hospital.....	Minneapolis, Minn.
Veterans Administration Hospital.....	Brooklyn, N. Y.
Veterans Administration Hospital.....	Montrose, N. Y.
Veterans Administration Hospital.....	Nashville, Tenn.
Veterans Administration Hospital.....	Seattle, Wash.
Arkansas State Hospital.....	Little Rock, Ark.
Halstead Hospital.....	Halstead, Kan.
Central State Hospital.....	Lakeland, Ky.
St. Mary's Group of Hospitals.....	St. Louis, Mo.
St. Lawrence Hospital.....	Ogdensburg, N. Y.
State Hospital.....	Raleigh, N. C.
Beverly Hills Clinic and Sanitarium.....	Dallas, Texas

Surgery

Veterans Administration Hospital ¹	Little Rock, Ark.
Veterans Administration Hospital ²	Seattle, Wash.
Mercy Hospital ³	Iowa City, Iowa
Edward W. Sparrow Memorial Hospital ²	Lansing, Mich.
Beth David Hospital ¹	New York, N. Y.
Rex Hospital ¹	Raleigh, N. C.

Thoracic Surgery

Veterans Administration Hospital.....	Brooklyn, N. Y.
Ingham Sanatorium.....	Lansing, Mich.

1. Approved for three years of training by the Council, the American Board of Surgery, and the American College of Surgeons, through the Conference Committee on Graduate Training in Surgery.
2. Approved for four years of training by the Council, the American Board of Surgery, and the American College of Surgeons, through the Conference Committee on Graduate Training in Surgery.
3. Approved by the Council as offering satisfactory training of one or two years' duration, in preparation for residency training in the surgical specialties (Approved Programs in Surgery, J. A. M. A. 142: 1210 [April 15] 1950).

COUNCIL ON NATIONAL
EMERGENCY MEDICAL SERVICE

At its meeting in Chicago on Feb. 10, 1952, the Executive Committee of the Council on National Emergency Medical Service discussed in detail the current and future needs of the armed services for additional medical personnel. Following is a brief statement of the facts disclosed in this regard and the position adopted by the Committee.

C. JOSEPH STETLER, Secretary.

MEDICAL PERSONNEL FOR ARMED SERVICES

Despite conflicting reports as to the requirements of the armed services for medical personnel, it now appears that there is no need at present for any appreciable number of additional physicians. In actuality, the present lull in the fighting in Korea, owing to peace negotiations, has resulted in an extremely low number of casualties and consequently a temporary excess in the number of physicians.

It is realized, of course, that the exigencies of the current situation make it impossible to reduce immediately the number of medical and allied health personnel in Korea and Japan. Nevertheless, it is apparent that, if the truce talks are successful and if hostilities are not resumed, a substantial number of physicians and nurses could and would be brought back to the United States from the Far East within a short period. These facts were substantiated by a report presented by Major General George E. Armstrong, Surgeon General of the Army, at a meeting of the Joint Committee on Medical Education in Time of National Emergency held in Chicago on Feb. 9, 1952. General Armstrong recently returned from a tour of Korea and the Far East.

It was the opinion of the Executive Committee of the Council that these facts were sufficient to justify the following conclusions. 1. The induction of physicians and allied specialists under the Universal Military Training and Service Act, as amended, and the recall of reserve medical personnel can be curtailed. 2. It may soon be possible to discharge a substantial number of such persons from the armed services and return them to civilian life.

At the time of the enactment of Public Law 779, 81st Congress, "The Doctor Draft Law," in September, 1950, there was a critical need for physicians in the armed services that was not being met. It was felt necessary, therefore, to pass legislation that would establish machinery for channeling physicians into the armed services on an equitable basis. The priorities under Public Law 779 were designed by the Congress to call into service first those men with the greatest obligation to serve. These priorities were established with particular consideration being given to deferments during World War II to complete medical training, the receipt of all or a part of medical education at government expense, and the length of services during World War II.

Despite their original endorsement of the Doctor Draft Law, the Council on National Emergency Medical Service and the American Medical Association are, of course, extremely anxious for the termination of the need for such legislation. As long as the situation in Korea remains as it is at present, it should be necessary only to replace the medical officers who are being discharged upon completion of their statutory tours of duty. A final termination of hostilities should further reduce this need for medical replacements to a small percentage of current requirements.

When the extreme need for medical personnel in the armed services became apparent following the Korean incident, the Council felt that it was the patriotic duty of individual physicians and the medical profession as a whole to see that this need was satisfied. It feels equally strongly, however, about the absolute necessity of returning these physicians to civilian life as soon as the needs of the armed services are in any way reduced.

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Arch. Dermat. and Syphilol., Chicago

64:667-812 (Dec.) 1951

- *Dermatological Problems Among Pharmaceutical Workers. J. E. Dalton and J. D. Peirce.—p. 667.
- *Treatment of Lupus Vulgaris by Intralesional Injections of Calciferol: Its Use in Localized, Recurrent, or Refractory Cases. B. Russell.—p. 676.
- Sulfoxone (Diasone®) Sodium for Dermatitis Herpetiformis. T. Cornbleet.—p. 684.
- Effect of "Aminopterin" on Epithelial Tissues. R. Gubner.—p. 688.
- Studies in Histogenesis of Epidermis. F. J. Eichenlaub and R. A. Osbourn.—p. 700.
- Histoplasmin Sensitivity in Panama Canal Zone: Correlated Clinicopathologic Study of 1,000 Patients, with Speculations as to Present Status of Histoplasma Capsulatum on Isthmus of Panama. H. A. Tucker.—p. 713.
- Pemphigus: Histologic Study. W. F. Lever.—p. 727.
- Clinical Evaluation of "Diphenylpyraline" as Antifungal Agent. O. Sokoloff.—p. 754.
- Use of Aureomycin in Case of Osteoperiostitis of Syphilis. F. W. Crowe and S. A. M. Johnson.—p. 757.
- Lymphocytoma of Skin: Report of Unusual Case (Lymphocytoma Tumidum). M. Waisman and R. G. Olivetti.—p. 761.
- Piedra: Report of Case. M. J. Scott.—p. 767.
- Metastatic Cutaneous Carcinoma from Breast: Clinical and Pathological Study of Case Showing Three Types of Lesions. U. W. Leavell Jr. and F. W. Tillotson.—p. 774.

Dermatoses in Pharmaceutical Workers.—It is widely believed that the incidence of occupational dermatoses is high in the pharmaceutical industry, because workers in this field are exposed to primary irritants or sensitizers of the skin. The authors of this paper studied the dermatological problems that occurred among 5,514 employees of a pharmaceutical company between Nov. 1, 1948, and Nov. 1, 1950. Early in this study period, some skin lesions were designated occupational or nonoccupational solely on the basis of the history; later however, patch testing was done in 322 cases, and 43 positive reactions were obtained. Among 91 persons who were referred for consultation there were reactions to 126 different substances. Nonoccupational causes accounted for 75% of these cases. Twenty-two workers had occupational dermatitis, but 6 of the 22 did not have an industrial dermatitis in the strict sense of that term. The records of all who showed a work-associated skin ailment were analyzed to determine the duration of an incubation period. Among employees working with antibiotics, it seemed that those working with penicillin worked longer before a reaction developed than those handling streptomycin. Yet there were fewer sensitizations to streptomycin than to penicillin. Likewise, workers with chemical agents showed a great variability in the period between their initial contact with an offending agent and the onset of skin symptoms. In all but three cases, eruptions occurred only in exposed areas of the skin. No worker had to leave the employment because of dermatitis.

Intralesional Injections of Vitamin D₂ in Lupus Vulgaris.—Russell describes his experiences with intralesional injections of vitamin D₂ (calciferol) in nine patients with lupus vulgaris. Clinical clearance resulted in six patients, five of whom had no lesions after 12 months, while the sixth relapsed after 13 months but

obtained clearance again after a further course of injections. Two other patients are greatly improved, and one has proved resistant. The advantages of this treatment are its consistent effectiveness, the smaller total dosage required, and the resultant freedom from side-effects. Its chief disadvantage is the pain associated with the injections. It is impracticable for extensive lesions or for those involving cartilage, and it has not yet been employed for lesions involving the mucous surfaces. Intralesional injections of vitamin D₂ are indicated for (1) small localized lesions, particularly in children; (2) refractory lesions; (3) recurrent localized nodules; (4) patients intolerant to systemic calciferol; and (5) patients with concurrent pulmonary tuberculosis or cardiovascular or renal disease, or who are pregnant.

A.M.A. Arch. Indust. Hyg. & Occup. Med., Chicago

4:519-622 (Dec.) 1951

- Benzidine (4, 4'-Diaminobiphenyl) and Substituted Benzidines: Microchemical Screening Technic for Estimating Levels of Industrial Exposure from Urine and Air Samples. J. M. Glassman and J. W. Meigs.—p. 519.
- Study of Exposure to Benzidine and Substituted Benzidines in Chemical Plant: Preliminary Report. J. W. Meigs, R. M. Brown and L. J. Sciarini.—p. 533.
- Rehabilitation of Persons with Pulmonary Dust Disease. O. A. Sander.—p. 541.
- *Platinosis: Five-Year Study of Effects of Soluble Platinum Salts on Employees in Platinum Laboratory and Refinery. A. E. Roberts.—p. 549.
- Aldrin Poisoning in Man: Report of Case. E. J. Spiotta.—p. 560.
- Chylomicron Count as Indicator of Phosphorus Poisoning: Study Utilizing Experimental Animals. R. B. L. Fleming and G. H. Collings Jr.—p. 567.
- Toxicity of Di-(Acetyl Cyanide). J. F. Treon, F. R. Dutra and J. Cappel.—p. 573.
- Absorption and Excretion of Inhaled Fluorides. G. H. Collings Jr., R. B. L. Fleming and R. May.—p. 585.
- Occupational Diseases of Dentists. F. J. Orland.—p. 591.
- Institute of Occupational Health in Helsinki. L. Noro.—p. 597.

Platinosis.—The effects of soluble complex salts of platinum on 21 employees in a platinum laboratory and refinery were studied during a period of five years. The term platinosis has been coined by the author to describe these effects that in his opinion may be observed in every person exposed occupationally to soluble platinum salts. The etiological agent is usually sodium chloroplatinate dissolved in a spray that is inhaled or contacts the skin. In 12 (60%) of the patients studied this exposure produced varying degrees of irritation of the upper respiratory tract accompanied by typical allergic manifestations of the skin (dermatitis) and of the respiratory system (asthma); the remaining 8 (40%) were allegedly free of symptoms, but had the same inflammatory changes in the conjunctivas and the mucous membranes of the upper respiratory tract, with a tendency toward hypertrophy of lymphatic tissue, and the same relative lymphocytosis observed among the symptomatic patients. Platinosis appears to be a mild chemical irritation, with chronic inflammation of the entire respiratory tract, probably including an apparently harmless pulmonary fibrosis. Some employees had both the cutaneous and the respiratory type of symptomatic platinosis. No evidence of carcinogenicity or of increased incidence of other pulmonary diseases such as tuberculosis or pneumonitis was noted. Blonde and red-haired persons with blue eyes and thin, delicately textured skin were apparently more susceptible to symptomatic platinosis than swarthy persons. Preemployment scratch tests with dilutions of sodium chloroplatinate were unreliable in predicting future sensitivity because people who previously had not been exposed to soluble platinum salts were not sensitized by the test dose of the etiological agent. Prophylaxis included careful selection of employees to exclude allergy-prone persons, daily changes to thoroughly cleaned uniforms, application of skin protectants prior to exposure, and adequate exhaust ventilation. The best active treatment for symptomatic platinosis was to remove the victim from the platinum atmosphere as soon as practicable.

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Titles marked with an asterisk (*) are abstracted.

A.M.A. Arch. Ophthalmology, Chicago

46:601-714 (Dec.) 1951

- *Anticoagulant Therapy in Occlusive Vascular Disease of Retina. I. F. Duff, H. F. Falls and J. W. Linman.—p. 601.
 Compensation Maximum: New Glaucoma Sign in Aqueous Veins. H. W. Kleinert.—p. 618.
 Dark Adaptation in Perimetrically Blind Fields. H. P. Krieger and M. B. Dender.—p. 625.
 Some Aids in Ophthalmoscopy: Contact Glass; Transilluminating Procedures; Headlight Employed as Ophthalmoscope. M. G. Ross.—p. 637.
 Clinical and Autopsy Findings in Early Retrolental Fibroplasia: Report of Case. G. S. Tyner and W. C. Frayer.—p. 647.
 Variable Ophthalmoplegia Due to Angioneurotic Edema. W. E. Fry and N. S. Schleizinger.—p. 655.
 Occlusion of Central Retinal Vein. I. T. Mancall.—p. 668.
 Glaucoma: Review of Literature 1950-1951. H. G. Scheie.—p. 677.

Anticoagulant Therapy in Occlusive Vascular Disease of Retina.

—Duff and associates used bishydroxycoumarin U. S. P. (dicumarol®) and heparin in treatment of 47 patients with occlusive vascular disease of the retina. Thirty-six patients were hospitalized, and 11 were treated as outpatients. Four received only heparin, 27 received heparin and bishydroxycoumarin, and the remainder received only bishydroxycoumarin. Heparin was administered intravenously by intermittent injection or by continuous infusion. When used with bishydroxycoumarin, heparin was given until bishydroxycoumarin had reduced the prothrombin concentration to the desired therapeutic range. The condition of 12 of 26 patients with thrombosis of the central retinal vein improved, of 8 remained unchanged, and of 6 grew worse. Four of the seven patients with tributary vein thrombosis showed improvement. Of the seven patients with lesions of the retinal arteries, only two improved. Of the 14 with diabetic retinopathy, 7 improved in visual acuity. Bishydroxycoumarin caused bleeding in 13 of the 47 patients, which in seven patients was sufficiently severe to require termination of the therapy. The prognosis for visual acuity following untreated thrombosis of a retinal vein is discouraging. In 79 untreated patients with complete occlusion of a central retinal vein, the condition grew worse in about half, and secondary glaucoma developed in 43%; only 15% showed improvement, and the condition remained unchanged in 35%. Anticoagulant therapy produced improvement in 54 of 93 patients, and the frequency of secondary glaucoma was reduced. However, the visual acuity of 19% remained unchanged, and that of 9% grew worse. A short term of intensive treatment with heparin appears to produce results as favorable as those obtained with prolonged use of bishydroxycoumarin. Since hemorrhage occurs frequently in long-term treatment with bishydroxycoumarin, heparin is recommended for general use. Treatment must be instituted promptly after thrombosis or occlusion of a retinal artery.

A.M.A. Arch. Pathology, Chicago

52:489-574 (Dec.) 1951

- *Polyarteritis Nodosa, Associated with Malignant Hypertension, Disseminated Platelet Thrombosis, "Wire Loop" Glomeruli, Pulmonary Silicotuberculosis, and Sarcoidosis-Like Lymphadenopathy. W. St. C. Symmers and R. Gillett.—p. 489.
 Thromboembolic Pulmonary Arteritis and Vascular Sclerosis: Its Experimental Production in Rabbits by Means of Intravenously Injected Human Amniotic Fluid and Autogenous Blood Clots. E. E. Muirhead and P. O'B. Montgomery.—p. 505.
 Metastasis to Pineal Body. P. Ortega, N. Malamud and M. B. Shimkin.—p. 518.
 Study of Tissue Implantations on Embryonated-Eggs Membranes. G. Saccomanno and R. Waldapfel.—p. 529.
 Cholesterol in Plasma and Tissues Subsequent to Its Intravenous Injection. M. Osborn, N. Womack, K. Daum and W. Kridelbaugh.—p. 546.
 *Ruptured Congenital Aneurysms of Aortic Sinuses of Valsalva: Report of Case with Bacterial Endocarditis Due to Hemophilus Parainfluenzae. F. J. Tenczar, R. J. Johansmann and J. Kaufman.—p. 552.

Periarteritis Nodosa.—The occurrence of periarteritis nodosa with several unusual pathological features is reported in a 54-year-old metal grinder whose death resulted when an aneurysm perforated in the duodenum. Necropsy revealed necrotizing arteritis and arteriolitis, with multiple large aneurysms on visceral arteries. Microscopically these lesions had the characteristic appearance of periarteritis nodosa. Clinical evidence of arterial hypertension was reflected microscopically in widespread hypertensive arteriolosclerosis and by histological evidence of

malignant hypertension. Certain changes usually associated with disseminated lupus erythematosus were also present, although there were no cardiac lesions and no history or evidence of dermatosis. Platelet thrombosis affected many smallest-caliber blood vessels. Unequivocal manifestations of the platelet thrombosis syndrome were not noted during life. Nodular pulmonary silicosis was associated with chronic, fibrocaceous pulmonary tuberculosis; acute, necrotizing tuberculous pneumonia had developed. A generalized lymphadenopathy presented lesions microscopically identical with the late sclerotic stage of sarcoidosis; no other lesions of this type were observed. It is somewhat difficult to postulate an etiological relationship between the tuberculosis and both periarteritis nodosa and the concomitant sarcoidosis-like affection, if the hypotheses of the respectively "hyperergic" and "anergic" nature of the two latter conditions are valid. The lymphadenopathy, however, did not have the microscopic appearances of active, progressing sarcoidosis, but had reached the advanced sclerotic stage and seemed to be almost "burnt out"; it was obviously of much greater age than the arteritis. If, therefore, the periarteritic and sarcoidosis-like lesions are considered morphological manifestations of opposite and noncontemporary phases of allergic reactivity to the same infection, it seems possible that both conditions had a common fundamental cause, the presence of tuberculous infection.

Ruptured Congenital Aneurysm.—Congenital aneurysms involving the right sinus of Valsalva perforating into the pulmonary conus and the noncoronary aortic sinus rupturing into the right atrium were revealed by necropsy in a Negro, aged 39, who died of bacterial endocarditis involving the pulmonary valve due to *Hemophilus parainfluenzae*. Congenital aneurysms of the sinuses of Valsalva are rare. The pathological findings in this case indicated that a defect in the development of the aortopulmonary septum with subsequent formation and rupture of aneurysms of the right and noncoronary aortic sinuses was the cause of the observed cardioaortic fistulas. This concept was confirmed by demonstration of an orderly lamination of elastic fibers in the proximal wall of the aortatrial fistula, the slight outward curving of the aortic elastica at the mouth of the aortopulmonary conal fistula, and the defect of elastica in the wall of the right aortic sinus between the mouth of the fistula and the annulus fibrosus. In addition, the orifices of the fistulas were situated where congenital defects tend to occur, since the right and noncoronary aortic sinuses are developmentally related to the septum that separates the conus and truncus arteriosus. Factors usually responsible for occurrence of an acquired aneurysm, such as syphilis, trauma, and atherosclerosis, were lacking. The endocarditis was considered a complicating rather than an etiological factor.

American Heart Journal, St. Louis

42:801-956 (Dec.) 1951

- Cardiac Beriberi Simulating Arteriosclerotic Heart Disease. P. Schlesinger and A. B. Benchimol.—p. 801.
 Coexistence of Rheumatic and Arteriosclerotic Heart Disease in Patients Over the Age of 40 Years. J. Chasnoff and A. Silver.—p. 809.
 Cardiovascular Disease in Marfan's Syndrome. R. J. Marvel and P. D. Genovese.—p. 814.
 Photoelectric Method for Determination of Arterial Oxygen Saturation in Man. P. Sekelj, A. L. Johnson, H. E. Hoff and M. P. Schuerch.—p. 826.
 Electrocardiographic Abnormalities in Patients Exhibiting Anxiety. H. Magendantz and J. Shortsleeve.—p. 849.
 Frontal Plane Ventricular Gradient in Induced Human Right Bundle Branch Block. N. O. Fowler Jr. and R. N. Westcott.—p. 858.
 *Tromexan in Treatment of Coronary Thrombosis. J. A. Tulloch and A. R. Gilchrist.—p. 864.
 Effect of Cortisone on Electrocardiograms of Normal Rabbits. W. B. Abrams and T. N. Harris.—p. 876.
 Improved Esophageal Lead for Electrocardiograph. R. H. Thayer and R. F. Foster.—p. 884.

Ethyl Biscoumacetate in Coronary Thrombosis.—The use of anticoagulants in the first few weeks after an acute coronary thrombosis marks a distinct advance in treatment. Since there are disadvantages in use of other available anticoagulant drugs, Tulloch and Gilchrist decided to use ethyl biscoumacetate (tromexan®) after other investigators had emphasized its faster absorption. They used ethyl biscoumacetate in treatment of 87

patients admitted to the hospital because of acute myocardial infarction. The routine treatment for all cases consisted in bed rest for five to six weeks, morphine at the outset for relief of distress, subsequent sedation with small doses of phenobarbital, a low calorie diet, graduated exercises from the fourth week, and symptomatic treatment of complications. The ethyl biscoumacetate was used alone in 11 patients. It was combined with heparin according to a definite scheme in 76 patients. It was found that ethyl biscoumacetate administered during the first four weeks after a coronary thrombosis in a dose sufficient to maintain the prothrombin time at a figure two to two and one-half times the normal value is an efficient substitute for bishydroxycoumarin (dicumarol[®]). By its use the mortality rate during the first six weeks was halved, falling from the 40.5% observed in a previous control series to 18.4%. This compares favorably with the 22.8% mortality among a bishydroxycoumarin-treated group. The relatively high mortality rates are largely attributable to the high proportion (nearly 60%) admitted to the hospital within 48 hours of the development of the myocardial infarct. Death is most common in the early days after the attack. Use of the drug reduces the incidence of thromboembolisms from approximately 1 in every 4 patients in control groups to less than 1 in 20 among the patients treated with ethyl biscoumacetate. Heart failure and sudden death now account for most of the fatalities. Ethyl biscoumacetate is a safer drug than bishydroxycoumarin; its shorter action and larger daily dose permit easier regulation of the anticoagulant therapy. The risk of prolonged overdosage with the associated hemorrhagic tendency is correspondingly reduced.

American Journal of Psychiatry, New York

108:401-480 (Dec.) 1951

- *Traumatic War Neuroses Five Years Later. S. Futterman and E. Pumpian-Mindlin.—p. 401.
- Long-Term Study of Combat Area Schizophrenic Reactions: Preliminary Report. H. S. Ripley and S. Wolf.—p. 409.
- Follow-Up Study of Psychoneuroses: Preliminary Report. N. Q. Brill and G. W. Beebe.—p. 417.
- Central Mechanism of Emotions (Experiences with Circumscribed Thalamic Lesions). E. A. Spiegel, H. T. Wycis, H. Freed and C. Orchinik.—p. 426.
- Emotions and Biochemical Findings in Alcoholism. M. F. Fleetwood and O. Diethelm.—p. 433.
- Rheoscopic Studies of Expression: Methodology of Approach. E. W. Straus.—p. 439.
- Transorbital Lobotomy in Chronically Disturbed Patients. W. W. Wilson, A. R. Pittman, R. E. Bennett and R. S. Garber.—p. 444.
- Physiological Responses to Heat Stress and ACTH of Normal and Schizophrenic Subjects. M. Stein, E. Ronzoni and E. F. Gildea.—p. 450.
- Utilizing the Community as a Therapeutic Resource. L. G. Sewall and C. W. Grady.—p. 456.
- Observations on Cultural Psychiatry During World Tour of Mental Hospitals. H. R. Gold.—p. 462.
- Prediction of Juvenile Delinquency Using the Minnesota Multiphasic Personality Inventory. S. R. Hathaway and E. D. Monachesi.—p. 469.

Traumatic War Neuroses Five Years Later.—This paper presents a summary of experiences with a large group of cases of traumatic war neurosis during the five-year period following World War II. Traumatic war neuroses occur relatively frequently in noncombatant military personnel in combat areas. This group is vulnerable because they are exposed to trauma without opportunity for effective motor discharge of the resultant emotions. Guilt about killing or assailing defenseless enemy personnel, either military or civilian, is an important factor in the precipitation of a traumatic war neurosis. In such instances the superimposed military code (superego) yields to the earlier and stronger civilian prohibition against violence toward others. Traumatic war neurosis can occur in conjunction with physical injury, since the resulting separation from the unit removes the influence of group morale as a deterrent to neurotic breakdown. Furthermore, enforced immobilization seems to encourage development of traumatic war neurosis by depriving the individual of the possibility of discharge of tension through motor activity. Overidealization of the pretraumatic history occurs in cases of traumatic war neurosis. This is a defensive maneuver of the ego in its effort to find some stable point in a world that has become overwhelming and threatening. The authors have not found intravenous narcosis or hypnosis particularly helpful in chronic

traumatic war neurosis. They differentiate two character groups among their patients with traumatic war neurosis, according to the pretraumatic adjustment. In the alloplastic, or outgoing, group therapy is usually relatively short and consists essentially of relating combat experiences to present feelings and attitudes. In the autoplasmic, or inhibited, group a further step can be taken in that the traumatic experiences are related not merely to their present feelings and attitudes but also to the pretraumatic experiences. This differentiation is important from a practical therapeutic point of view.

American Journal of Tropical Medicine, Baltimore

31:673-874 (Nov.) 1951. Partial Index

- New Criterion for Selection of Compounds for Curative Activity in Plasmodium Vivax Malaria. L. A. Terzian, P. A. Ward and N. Stahler.—p. 692.
- Intravenous Amodiaquin (Camoquin) in Naturally Acquired and Induced Malaria. E. H. Payne, V. M. Villarejos, E. A. Sharp and others.—p. 698.
- Experiences with Amodiaquin (Camoquin), New Synthetic Antimalarial. V. M. Villarejos M.—p. 703.
- Chemotherapy of Amebic Hepatitis in Hamsters with Emetine, Chloroquine, Amodiaquin (Camoquin), Quinacrine and Other Drugs. P. E. Thompson and J. W. Reinertson.—p. 707.
- Endamoeba Gingivalis in Pulmonary Suppuration. W. D. Sutliff, F. D. Green and L. S. Suter.—p. 718.
- Histoplasmosis and Pulmonary Calcification—Geographic Distribution. A. Christie.—p. 742.
- Histoplasmosis: Fourth Case Report from the Canal Zone. J. H. Draheim, J. R. Mitchell and N. W. Elton.—p. 753.
- Experimental Transmission of Tularemia by Tropical Rat Mite. C. E. Hopla.—p. 768.
- Studies of Diffusion of Water Through Dead Human Skin: Effect of Different Environmental States and of Chemical Alterations of Epidermis. G. S. Berenson and G. E. Burch.—p. 842.

Arizona Medicine, Phoenix

8:1-92 (Nov.) 1951

- Surgical Treatment of Esophageal Lesions. D. L. Paulson.—p. 27.
- Cholecystectomy Without Drainage. C. G. Fraser, J. E. O'Hare and G. M. Bogardus.—p. 32.
- What to Know About Carcinoma of Lung. R. M. Janes.—p. 36.
- Unusual Varieties of Pneumonia and Pulmonary Abscess. J. S. Chapman.—p. 38.

Geriatrics, Minneapolis

6:347-432 (Nov.-Dec.) 1951

SYMPOSIUM ON GERIATRIC GYNECOLOGY

- Uterine Tumors in Relation to Senescence. M. E. Davis.—p. 349.
- Dermatologic Problems of Aging Women. A. E. Palmer.—p. 363.
- Displacements of Uterus. H. P. Wager.—p. 379.
- Involutional Psychoses. P. Polatin and J. F. McDonald.—p. 391.
- Pregnancy After 40. J. Parks.—p. 399.
- Role of a Clinical Psychologist in a Home for the Aged. W. G. Klopfer.—p. 404.

Journal of Gerontology, St. Louis

6:327-444 (Oct.) 1951

- Calcification of Left Annulus Fibrosus. T. Geill.—p. 327.
- Interpretation of Calculated Changes in Renal Resistance with Age. M. Landowne and N. W. Shock.—p. 334.
- Litter Seriation Phenomena in Fibrosarcoma Susceptibility: Contribution to the Subject of Cancer Susceptibility in Relation to Age. L. C. Strong.—p. 340.
- Studies in Experimental Atherosclerosis: IV. Theoretic and Practical Implications of Results of Intravascular Injections of Cholesterol Sols. O. J. Pollak and B. Wadler.—p. 358.
- Differential Decline in Wechsler-Bellevue Subtests in Senile Psychoses. J. Botwinick and J. E. Birren.—p. 365.
- Excretion of Pantothenic Acid in Patients with Achromotrichia and Alopecia. V. Schmidt.—p. 369.
- *Effect of Work Program on Adjustment Attitudes in an Aged Population. R. W. Kleemeier.—p. 372.
- Social Role in Prevention of Senility. R. Albrecht.—p. 380.

Effect of Work on Adjustment in the Aged.—Programs of employment of residents have been tried in homes for the aged. To find out whether such a program benefits the individual, a survey was made of the activities and attitudes of residents of a fraternal home for the aged. The analysis was limited to men, chiefly because there were relatively few women residents. Of

the men, 56% were workers and 44% nonworkers. It has been estimated that to equal the part-time work of the residents in this institution would require more than 70 additional full-time employees on the staff. Thus the economic importance of the work program is obvious. That the work is meaningful rather than made-work is indicated by the list of jobs held by the residents: cook, kitchen helper, dining room helper, yard man, janitor, watchman, hospital orderly, truck driver, farm hand, barber, shopkeeper, carpenter, joiner, painter, plumber, meat-cutter, postman, and practical nurse. Participation in the work program is strongly encouraged but is voluntary. While both workers and nonworkers receive money allowances, those for the workers are greater and vary with the type of work and time spent. A psychological adjustment inventory was given to workers and nonworkers and it was found that (1) workers obtained higher scores than nonworkers of comparable health status; (2) both workers and nonworkers who rated their health good or fair obtained higher scores than those who rated their health poor; and (3) workers earned higher scores than nonworkers on subscales of the adjustment attitude inventory dealing with the areas of health, work, feelings of usefulness, and happiness. The author feels that, although only limited generalizations can be made on the basis of these data, the work program contributes something more than the mere doing of necessary jobs; it promotes the happiness and adjustment of those who participate.

Journal Nat. Cancer Inst., Washington, D. C.

12:259-464 (Oct.) 1951. Partial Index

- Metabolism of Hodgkin's Disease Tissue. H. Laser.—p. 259.
 Histology of Early Reactions of Skin and Mucous Membrane of Lip of Mouse to Single Application of Carcinogen. B. M. Levy, R. Gorlin and R. Gottsegen.—p. 275.
 Fertility and Cancer of Breast and of Uterine Cervix: Comparisons Between Rates of Pregnancy in Women with Cancer at These and Other Sites. A. G. Gilliam.—p. 287.
 Chemotherapy of Tumors in Rats: I. Treatment of Sarcoma 231 in King A Rat with 2, 4, 6-Triethylenimino-S-Triazine and Related Products. M. L. Crossley, J. B. Allison, W. W. Wainio and J. B. Muenzen.—p. 305.
 Electrophoretically Determined Blood-Protein Levels in Case of Acute Myelogenous Leukemia Under Exchange Transfusion Treatment. F. J. Gutter, J. R. Krevans, G. A. Moulton and G. Kegeles.—p. 323.
 Tumor Development in Backcross Mice Segregated with Respect to Hairless and Pink-Eye Genes. W. E. Heston and M. K. Deringer.—p. 361.
 Failure of Bile as Abetting Agent for 2-Methylcholanthrene in Induction of Gastric Tumors in Mice. C. R. Hitchcock.—p. 369.
 Vascular Reactions of Normal and Malignant Tissues in Vivo: IV. Effect of Peripheral Hypotension on Transplanted Tumors. G. H. Algire and F. Y. Legallais.—p. 309.
 Further Observations on Inhibition of Lymphoid Tumor Development by Shielding and Partial-Body Irradiation of Mice. H. S. Kaplan and M. B. Brown.—p. 427.

New England Journal of Medicine, Boston

245:793-832 (Nov. 22) 1951

- Report of Cancer Detection Center Demonstration in Massachusetts. H. L. Lombard, C. C. Franseen, L. S. Snegireff and E. A. Potter.—p. 793.
 Adrenocortical Function in Pernicious Anemia. M. B. Strauss and R. Brokaw.—p. 798.
 Severe Hemorrhage Due to Tromexan: Report of Three Cases. R. P. Gripe.—p. 803.
 *Prolonged Cation-Exchange Resin Therapy in Congestive Heart Failure. C. Voyles Jr. and E. S. Orgain.—p. 808.
 Electrolyte and Fluid Disturbances in Congestive Heart Failure. C. K. Friedberg.—p. 812.

245:833-874 (Nov. 29) 1951

- Appraisal of Newer Electrocardiography: Correlations in 150 Consecutive Autopsied Cases. H. D. Levine and E. Phillips.—p. 833.
 Inhalation of Ethyl Alcohol for Pulmonary Edema. A. Gootnick, H. I. Lipson and J. Turbin.—p. 842.
 Gastric Ulcer in the Preschool Child: Report of Case. J. J. Goldsberry.—p. 844.
 Hypopotassemia in Untreated Diabetic Coma. S. M. Perry and S. L. Rosenbaum.—p. 847.
 Electrolyte and Fluid Disturbances in Congestive Heart Failure. C. K. Friedberg.—p. 852.

Cation-Exchange Resin Therapy in Heart Failure.—Three ambulatory patients had long-standing chronic cardiac decompensation that was uncontrolled by the usual therapeutic measures, including rest, rigid sodium restriction, digitalization, and mer-

curial diuresis. These patients were studied during continuous administration of cation-exchange resin for five to nine months. Each patient showed improvement while taking resin, as evidenced by stability of weight, absence of edema, improved exercise tolerance, and lowered requirement of mercurial diuretics. Extremely low urinary sodium-excretion levels were noted, but no serious serum-electrolyte disturbances were observed. No unfavorable signs were encountered despite the concomitant use of relatively strict low-sodium diets and resin but such patients must be observed carefully for signs of azotemia, acidosis, hypocalcemia, hypokalemia, hyperkalemia, and the low-sodium syndrome. It is concluded that prolonged continuous or intermittent use of a cation-exchange resin is a useful adjunct to treatment of congestive heart failure. It is believed that compensation would not have been possible in these cases without the use of a cation-exchange resin.

New Orleans Medical and Surgical Journal

104:213-252 (Dec.) 1951

- Recent Advances in Treatment of Cervical Cancer. A. N. Arneson.—p. 213.
 *Vulvovaginitis. J. H. Collins and C. J. Ellington Jr.—p. 220.
 Urological Conditions Related to Gynecology. E. E. Dilworth, C. R. Mays and C. C. Locke.—p. 228.
 Multiple Simultaneous Unilateral Tubal Pregnancy: Case Report. R. Kap-sinow.—p. 232.
 Urinary Tract Infection in Children. J. M. Baty.—p. 234.
 Treatment of Hypospadias. E. Burns and B. M. Harvard.—p. 237.
 Congenital and Infantile Aphasia: Review of Literature and Report of Case. D. W. Van Gelder, L. Kennedy and J. Lagaite.—p. 241.

Vulvovaginitis.—The terms vaginitis and vulvitis are applied to any abnormalities observed in these organs. Local factors as well as systemic abnormalities may play a part in vulvovaginitis. An accurate history is of great importance. Systemic diseases that must be considered include diabetes, nutritional deficiencies, jaundice, diseases of the skin, and diseases of the central nervous system. Allergies and the patient's occupation with reference to exposure to dusts or chemicals, clothing, and the type of material with emphasis on the synthetic cloths, particularly nylon, must be investigated, as well as the patient's habits relative to drugs, laxatives, contraceptives, douches, deodorants, perfumes, and powders. Former treatments must be inquired into, with emphasis on douches, ointments, jellies, hormones, antibiotics, and last, but by no means least, whether or not the patient has been subjected to radium or x-ray treatment of the vulva. The pubic and vulval areas must be inspected under a good light. Ulcerative lesions are investigated with smears, darkfield examinations of cultures, and serologic tests. Nonulcerative neoplastic lesions necessitate biopsy. Urinary continence is checked, and the cervix, uterus, tubes, and ovaries are evaluated. The treatment must consider the cause. Diabetic vulvitis will resist any and all forms of topical treatment, while control of the diabetes will effect cure. Faulty food habits and the elimination of excessive sugar from the diet frequently relieves patients who have no clinical or laboratory signs of diabetes. Good nutrition and supplemental vitamins, particularly the B complex and vitamin A, seem to have a beneficial effect on some forms of vulvitis and vaginitis. Psychological advice may help some of these patients. Urinary incontinence or fistulas need correction. Relief from pain or irritation can be secured temporarily with local applications of mild ointments, sitz baths, boric acid packs, and avoidance of irritation from clothing. Specific therapy is applied when the diagnosis of the causative agent has been established. Trichomonas vaginitis as well as mycotic vulvovaginitis resist treatment in a certain percentage of cases. No agent has been discovered that will cure all patients harboring these organisms. The authors believe that use of the douche is abused, and that many cases of vulvovaginitis are caused and prolonged by injudicious douching. Physicians should inform patients that with rare exception, douching is unnecessary and possibly even injurious. When necessary, plain water, saline, or mild acid douches may be used.

New York State Journal of Medicine, New York.

51:2551-2694 (Nov. 15) 1951

- Progress in Preventing Blindness. F. M. Foote and T. H. Johnson.—p. 2609.
- Sympathetic Ophthalmia, Its Pathogenesis and Prophylaxis. H. H. Joy.—p. 2613.
- Common Pitfalls in Ocular Surgery. I. J. Koenig.—p. 2617.
- Role of Heredity in Ophthalmology. H. F. Falls.—p. 2624.
- Excision of Extensive Lye Strictures of Esophagus. J. R. Paine.—p. 2628.
- Radical Surgery for Head and Neck Cancer. W. L. Watson.—p. 2631.
- Effect of ACTH and Cortisone on Upper Respiratory Tract. J. E. Bordley.—p. 2636.
- Expanding Tumors of Maxillary Sinus: Value of Lateral Rhinotomy. C. A. Heatly.—p. 2640.
- Orally Administered Citrovorum Factor in Treatment of Pernicious Anemia with Neurologic Complications. N. S. Moore, M. L. Scott, C. S. Wallace and G. Fiola.—p. 2645.
- New Concepts on "Brittle" Diabetes. H. Schwab.—p. 2647.
- A Proctoscopic Table. A. A. Kane.—p. 2650.
- Epival Soluble Anesthesia for Major Surgery. C. P. Boyan and O. Schweizer.—p. 2651.
- Psychosomatic Treatment of Obesity. W. Dorfman.—p. 2655.

Oklahoma State Medical Assn. J., Oklahoma City

44:459-508 (Dec.) 1951

- Clinical Use of Peritoneal Irrigation: Simplified Method and Its Indications. E. E. Muirhead.—p. 462.
- Low Bowel Obstruction—Roentgen Diagnosis. L. M. Pascucci.—p. 469.
- Appendicitis. R. G. Stoll.—p. 474.
- Medical Management of Ulcerative Colitis. T. Covington Jr.—p. 477.
- Adenoma of Large Bowel. J. D. Shipp.—p. 480.

Pediatrics, Springfield, Ill.

8:603-752 (Nov.) 1951

- *Effect of Adrenocorticotrophic Hormone on Rheumatic Fever. A. Dorfman, K. Smull, D. M. Bergenstal and others.—p. 603.
- Interpretation of Basal Metabolic Rate of Children of Unusual Body Build. A. Iliff, V. A. Lee and R. C. Lewis.—p. 616.
- *Atresia of Intrahepatic Bile Ducts. E. H. Ahrens Jr., R. C. Harris and H. E. MacMahon.—p. 628.
- Heat Prostration in Fibrocystic Disease of Pancreas and Other Conditions. W. R. Kessler and D. H. Andersen.—p. 648.
- Splanchnicectomy for Pancreatic Fibrosis: Analysis of Results in 24 Patients. W. B. Ayers, D. Stowens, A. Ochser and R. V. Platou.—p. 657.
- Paroxysmal Hypertension Simulating Pheochromocytoma. N. Aronson, G. S. Stern and S. Q. Cohan.—p. 664.
- Vesicular Pharyngitis: Its Relationship to Coxsackie Group of Viruses. J. K. David Jr., D. Leavitt and B. F. Howitt.—p. 672.
- Asphyxial Attacks in the Newborn Infant Due to Congenital Occlusion of Posterior Nares: Report of Five Cases. H. Medovy and I. H. Beckman.—p. 678.
- Sexual Precocity in Females: Report of Two Cases, with Arrest of Precocity in McCune-Albright Syndrome After Removal of Cystic Ovary. L. G. Pray.—p. 684.
- Epiphyseal Injuries in Breech Delivery. B. H. Shulman and C. B. Terhune.—p. 693.
- The Testis: V. Use of Testicular Biopsies in Differential Diagnosis of Precocious Puberty. E. H. Sobel, R. C. Sniffen and N. B. Talbot.—p. 701.

Corticotropin in Rheumatic Fever.—Of 22 children between the ages of 3½ and 15 years with rheumatic fever treated with corticotropin (ACTH), 3 had acute rheumatic fever, 8 had acute rheumatic fever associated with pancarditis, and 11 had chronic rheumatic fever. All patients had elevated erythrocyte sedimentation rates and signs of carditis. Treatment with corticotropin was generally started with a dose of 80 mg. per day administered intramuscularly in four equally divided doses every six hours. The daily dose was reduced to 40 mg. after two days. It was kept at this level for most of the period of treatment that varied from four to six weeks, and it was finally decreased further before treatment was discontinued. Arthritis occurred so infrequently that evaluation of therapy was impossible. Of the 22 patients, 19 showed a significant elevation of temperature preceding treatment and 16 showed a definite drop in temperature during treatment. The three patients whose temperature was not affected by treatment had pancarditis and died during treatment. The incidence of rheumatic skin rashes was too low to draw any final conclusions as to the effect of drugs. Nodules were present in only three patients and disappeared during treatment. Except in the 4 patients who died during treatment, a striking decrease in sedimentation rate was observed. The time required for the sedimentation rate to return to normal varied from 10 to 14 days. This measurement was the most convenient index

for follow-up of the patients and in general correlated with clinical remissions. One of the most striking changes in the carditis was the disappearance of pericardial friction rubs in all but the patients who died during therapy. The time required for disappearance of such evidence of pericarditis varied from a few days to two weeks. Tachycardia was present in all patients but, except in those who died, the pulse rate returned to normal during treatment. In 13 patients with congestive failure previous to therapy, evidences of congestive failure had disappeared before the cessation of therapy. No patient of this group has had a recurrence of congestive failure subsequent to therapy. The changes observed in the various manifestations of carditis suggested that corticotropin exerts a definite effect on carditis. In almost all of the patients there was evidence of reactivation of disease on withdrawal of drug. Corticotropin therapy did not prevent death due to acute rheumatic pancarditis in every case. There is no indication of whether treatment of active rheumatic fever with corticotropin changes the incidence of late valvular deformities.

Atresia of Intrahepatic Bile Ducts.—The occurrence of atresia of the intrahepatic bile ducts is reported in three girls who died between 3 and 3½ years of age, and one boy who was still alive at the age of 6½ years. Of the four, three also had anomalies of the extrahepatic bile ducts. All had secondary biliary cirrhosis. The course of the disease was distinguished by a relatively long life span. Generalized skin xanthomatosis occurred in all patients, together with a pronounced and characteristic elevation of the serum lipids. Postmortem examination performed in the three fatal cases did not indicate that intrahepatic bile ducts had developed and then become obliterated. The evidence presented suggests that absence of interlobular bile ducts is a developmental anomaly, and that the embryologic development of biliary epithelium is normally independent of the growth of hepatic trabeculae.

Plastic and Reconstructive Surgery, Baltimore

8:335-416 (Nov.) 1951

- Application of Permanent Pedicle Blood-Carrying Flaps. J. B. Brown, M. P. Fryer and F. McDowell.—p. 335.
- Congenital Atresia of Oropharynx. J. J. Longacre.—p. 341.
- Clinical Dilemmas in Specialty Practice of Medicine. N. Owens.—p. 349.
- *ACTH in Plastic Surgery. H. Conway and R. B. Stark.—p. 354.
- Biology of Skin Graft: New Aspects to Consider in Its Revascularization. L. Mir y Mir.—p. 378.
- Treatment of Invertebrate Facial Paralysis. H. Brunner.—p. 390.
- New "Economic" Technic in Treatment of Hidrosadenitis of Buttocks. A. F. Borges.—p. 396.
- Fibrous Dysplasia of Maxilla. E. J. Hill.—p. 398.
- Simple Technic for Removal of Fine Interrupted Skin Sutures. A. P. Hovnanian.—p. 407.

Corticotropin in Plastic Surgery.—Reports that treatment with corticotropin (ACTH) limited the development of granulation tissue and fibrous tissue, stimulated epithelization, and improved the management of extensive burns and that homotransplants of skin were successful permanently after such treatment stimulated investigations on the use of corticotropin in plastic surgery. Observations are reported on the epithelization of wounds, homotransplants of skin, and treatment of keloids and burns. In a patient with Cushing's disease the formation of granulation and fibrous tissue was greatly inhibited. The rate of epithelization was delayed as compared in a control patient. In experimental animals homotransplantation of skin was unsuccessful, even though the animals were treated with corticotropin. However, the thromboses of minute vessels adjacent to the homoplastic grafts apparently were prevented in more than half of the experiments. Such thromboses had been observed regularly prior to the sloughing of homoplastic skin grafts in animals not treated with corticotropin. Their development had been looked on as one factor contributing to the failure of homoplastic transplants. A patient is described who was treated with corticotropin before and after homotransplants of skin, but the transplants did not take. In two patients the excision of keloids was followed by therapy with corticotropin; the keloids have not recurred in the eight months and five months, respectively, that have elapsed since excision. In four patients keloids were injected directly with a mixture of corticotropin and hyaluronidase. All patients were relieved of their

symptoms of pain and itching. In one case, the keloid was notably softer and less erythematous following treatment. There have also been reports of dramatic results obtained with corticotropin in the treatment of severe burns, but these favorable results were largely nullified by reports that serious complications and even deaths followed the sudden withdrawal of the hormone or were brought on by the side-effects of the hormone. It is believed that clinical research on the value of corticotropin should be continued.

Proc. Soc. Exper. Biol. & Med., Utica, N. Y.

78:363-664 (Nov.) 1951. Partial Index

- Abrupt Improvement of Serum Electrophoretic Pattern in Nephrosis After ACTH-Induced Diuresis. S. E. Lenke and H. M. Berger.—p. 366.
Preparation of Specific Complement-Fixing Antigen with Lansing Polio-myelitis Virus. M. Pollard.—p. 388.
Abnormalities in Offspring of White Rats Given Protamin Zinc Insulin During Pregnancy. H. Lichtenstein, G. M. Guest and J. Warkany.—p. 398.
Studies of Proteolytic Enzyme Systems in Patients with Emotional Disorders. J. S. L. Jacobs, P. M. West and C. E. Tempereau.—p. 410.
Some Pharmacological Properties of Three New Mercurial Diuretics. C. A. Handley, D. Chapman and J. H. Moyer.—p. 433.
Improvement of Protein Quality of Whole Wheat. R. Beaudoin, J. Mayer and F. J. Stare.—p. 450.
Chemical Inhibition of Decapsulation in Beta Hemolytic Streptococcus. L. M. Weiner and C. V. Seastone.—p. 466.
Modification of Sensitivity to X-Radiation by Morphine Sulfate. J. B. Kahn Jr.—p. 486.
Effect of Oral Terramycin Prior to Whole Body X-Radiation. G. E. Gustafson and S. Koletsky.—p. 489.
Effect of Adrenal Hormones on Infection of Mice with Pneumonia Virus of Mice (PVM). J. M. Smith, J. S. Murphy and G. S. Mirick.—p. 505.
Hemagglutination Reaction in Streptococcal Infections and Acute Rheumatic Fever. W. M. M. Kirby.—p. 519.
Proliferation and Vascularization of Adult Human Epithelium in Subcutaneous Tissues of X-Irradiated Heterologous Hosts. H. W. Toolan.—p. 540.
Recovery of Growth Hormone in Purification of Corticotropin. M. S. Raben and V. W. Westermeyer.—p. 550.
Aureomycin and Terramycin in Human Saliva. F. W. Kraus, D. W. Casey and V. Johnson.—p. 554.
Regulation of Breathing in Man at Altitude. F. G. Hall.—p. 580.
Hemodilution as Result of Estrogen Therapy: Estrogenic Effects in the Human Female. C. L. Witten and J. T. Bradbury.—p. 626.

Hemodilution Resulting from Estrogen Therapy.—Sixteen women from 15 to 52 years of age were given estrogens because of minor menstrual irregularities. The estrogen treatment and the blood studies were completed in the intermenstrual interval so none of the blood changes could be attributed to menstrual blood loss. Either 5 mg. of estrone or 0.4 mg. of α -estradiol dipropionate was given intramuscularly on alternate days for a total of two to four injections. The erythrocyte count, hemoglobin level, and hematocrit value were low during the 4 to 10 days in which estrogen was administered. On cessation of the estrogen therapy, there was a return to initial levels within five to nine days. Evans blue dye studies made in 3 of the 16 women demonstrated that the blood volume increased enough to account for the lowering of the red cell count, hemoglobin level, and hematocrit reading. These studies confirm observations of other investigators. The loss of blood volume following oophorectomy noted by Friedlander and associates and its correction by estrogen therapy suggests that the vasomotor symptoms of the surgical or natural menopause may be, in part, a reflection of blood volume changes. The hemodilution also suggests that the increased estrogen level during pregnancy may be a causative factor of the increased blood volume and the "physiologic anemia" that occurs in pregnant women. Studies in women who experience a definite premenstrual edema would be of interest to determine whether an intravascular fluid increase parallels the extravascular fluid increase. Hematological studies during therapy with estrogen and progesterone or testosterone would show whether these hormones modify or augment the action of estrogen.

Psychoanalytic Quarterly, Albany, N. Y.

20:511-682 (Oct.) 1951. Partial Index

- Some Etiological Aspects of Repression, Guilt and Hostility. A. McF. Johnson.—p. 511.
Anxiety and Organism. S. S. Feldman.—p. 528.
Childhood Attitudes Toward Filiality and Their Possible Relation to Adult Character. B. R. Merrill.—p. 550.
Concept of Defense. G. Gerö.—p. 565.

Southern Medical Journal, Birmingham, Ala.

44:1089-1180 (Dec.) 1951. Partial Index

- Problems in Diagnosis of Carcinoma of Lungs. S. W. Brown.—p. 1089.
*Pleuropulmonary Amebiasis. N. A. Kilgore Jr.—p. 1093.
*Physiologic Basis for Intra-Arterial Transfusion in Severe Hypotension. J. R. Veal, T. J. Dugan, R. Bauerfeld and A. S. Russell.—p. 1096.
Physical Medicine and Rehabilitation: Progress and Objectives in Veterans Administration. A. B. C. Knudson.—p. 1100.
Effect of Cortisone and ACTH in Corneal Dystrophy. J. Fulmer.—p. 1105.
Guillain-Barré Syndrome: Convalescent Treatment by Physical Measures. O. F. von Werssowetz.—p. 1106.
Comparative Studies in Penicillin Therapy of Early Syphilis. R. O. Noojin and M. V. Stallworth.—p. 1113.
Aureomycin, Oral, Intravenous and by Local Application in Treatment of Dermatoses. H. M. Robinson and H. M. Robinson Jr.—p. 1116.
Aureomycin in Male Trichomoniasis. L. V. McVay Jr., L. Evans and D. H. Sprunt.—p. 1122.
Treatment of Ascariasis with 1-Diethylcarbamyl-4-Methyl-Piperazine Hydrochloride. M. T. Hoekenga.—p. 1125.
Trichinosis: Its Prevalence, Diagnosis and Prevention. W. J. Senter.—p. 1127.
Therapy of Functional Uterine Bleeding. R. B. Greenblatt and W. E. Barfield.—p. 1131.
Indications for Surgical Intervention in Sterility of Female. B. B. Weinstein.—p. 1135.
Implantation of Salpinx Employing Cannula. V. D'Ingianni and I. L. Fontenelle.—p. 1139.
Central Neurofibromatosis: Report of Two Cases, One with Benign, Other with Malignant Multiple Neurogenous Tumors of Spinal Canal. J. M. Meredith.—p. 1143.
Cryptococcosis: Report of Three Cases. H. E. K. Sweeny and J. M. Rumball.—p. 1152.
Skin Graft in Treatment of Chronic Furunculosis of Posterior Surface of Neck (Folliculitis Keloidalis). F. F. Kanthak and M. L. Cullen.—p. 1154.
South's First Full Summer Camp for Diabetic Children and Observations on Use of NPH Insulin. J. S. Sweeney.—p. 1157.

Pleuropulmonary Amebiasis.—The pleuropulmonary complications of amebiasis should be considered more often in differential diagnosis of chest disease on the lower right side. In the past an erroneous diagnosis of tuberculosis, bronchiectasis, bronchopneumonia, lung abscess, or pleurisy with effusion was made frequently, and many patients were treated for these diseases for long periods before amebiasis was considered. The greatest diagnostic aid in pleuropulmonary amebiasis is having its possibility in mind. A present or past history of dysentery, especially if known to be amebic, and signs of liver tenderness and enlargement with pleural and pulmonary disease should make one consider amebiasis as probably present. If there is basal disease of the right lung, with elevation and fixation of the diaphragm and expectoration of large amounts of chocolate sauce pus, a positive diagnosis can be made. Primary pleuropulmonary infection is rare or doubtful as the reported cases are not too well proved. Pleuropulmonary involvement is probably always secondary to amebic infection somewhere in the gastrointestinal tract, the liver most frequently and colon less frequently. In 61 cases collected from the literature, there were 12 in which the pulmonary involvement was not associated with demonstrable liver involvement. Administration of emetine hydrochloride produces a dramatic cure, and chloroquine diphosphate is also effective and less toxic. The response to the administration of emetine hydrochloride or chloroquine diphosphate may be necessary, in some instances, to make a positive diagnosis or to determine which pulmonary lesion is amebic.

Intra-Arterial Transfusion in Severe Hypotension.—Perfusion experiments carried out on anesthetized dogs demonstrated that hemorrhage reduced the limb blood flow (perfusion) before it caused a decline in the systematic arterial pressure. They also revealed that, as the shock deepened, the circulation became totally inadequate and the heart could no longer contract effectively. In such a state it was observed that even the aortic valves became incompetent. The graded degrees of shock that had been established by bleeding the animals were then combated by blood transfusions. Comparisons were made of the effectiveness of replacing the blood by the intravenous and intra-arterial routes. The milder grades of hypotension were successfully overcome by either method. In the moderately severe stages both methods were effective, but the results were more rapid with intra-arterial administration. Smaller amounts of blood were required when it was given intra-arterially. In the graver states of hemorrhage, quantitative replacement of blood failed to over-

come the shock when given intravenously but did succeed when given intra-arterially. When hypotension reaches a critical stage, even large quantities of blood given intravenously may not restore the circulation. In fact it may cause complete failure by overloading the right side of the heart. To obtain forceful cardiac contractions and reestablish perfusion of the blood, the arterial pressure must be raised rapidly. This may be accomplished by intra-arterial transfusion. When blood is administered intra-arterially, at a pressure higher than that existing in the arterial bed, the blood will flow along the course of least resistance. It may fill the entire arterial system before an appreciable amount enters the veins. As soon as the aortic pressure is elevated, the intra-aortic resistance is increased and the heart pressure rises. This in turn allows better contractions and more forceful propulsion of blood into the aorta. By elevating the intra-arterial pressure the vasoconstriction is also relaxed and more adequate perfusion throughout the vascular bed results.

Stanford Medical Bulletin, San Francisco

9:205-292 (Nov.) 1951. Partial Index

- Studies in Subtotal Nephrectomy in Rats. L. J. Rafter.—p. 207.
Comparative Study of Metabolic Effect of Adrenocorticotrophic Hormone (ACTH), Cortisone, and Desoxycorticosterone Acetate (DCA). R. Luft and B. Sjögren.—p. 218.
Skeletal Evaluation of Portacaval Anastomosis for Gastrointestinal Hemorrhage in Cirrhosis of Liver. R. Cohn.—p. 231.
Antiviral Chemotherapy: V. Further Report on Flavonoids. W. E. Cutting, R. H. Dreisbach, M. Azima and others.—p. 236.
Effect of Fluorides in Acne Vulgaris. E. Epstein.—p. 243.
Heart Failure from Estrogen Therapy for Prostatic Carcinoma: Case Report. H. M. Weyrauch and M. L. Rosenberg.—p. 245.
Weight Reduction in Treatment of Diabetes Mellitus: Case Report. G. B. Robson.—p. 260.

Fluorides in Acne Vulgaris.—The use of fluorides as a prophylactic agent against dental cavities is widespread. However, one patient with acne vulgaris, who had a severe exacerbation of her pustular eruption, pointed out that she was taking a fluoride tablet as a preventative against dental caries. It seemed advisable to discontinue the use of fluoride in this patient, and a study was conducted to determine if fluoride tablets have any deleterious effects on the eruption of acne vulgaris. Lozenges containing calcium fluoride 0.002 gm., ascorbic acid 0.03 gm., vitamin D 400 U. S. P. units, and synthetic flavoring were given to 20 patients with acne. Once a day one lozenge was held in the mouth until dissolved. These were taken for from 1 to 11 weeks, the average being about 6 weeks. Other remedies were continued, since harmful rather than beneficial results were anticipated. In no instance did the acne lesions become severer while the patient was taking the fluoride lozenges, and 45% of the patients improved while receiving this medication. However, of 20 controls who received no fluoride lozenges, but otherwise the same treatment, 55% improved. The author feels that this study emphasizes the necessity of controls in evaluating therapeutic agents. On the face of it, the beneficial results obtained while the subjects were taking the fluoride lozenges approached those obtained with certain highly endorsed remedies for acne. However, comparison with the control series indicates that the lozenges studied neither irritated nor improved the eruptions.

Weight Reduction in Diabetes Mellitus.—In the case reported, a woman, aged 27, was hospitalized with a history of having been in coma for the previous eight hours. She had been having increasing urinary frequency for several weeks. After eight hours she had received 575 units of insulin, and her blood sugar level at this time was 260 mg. per 100 cc. Treatment was continued and after about 15 hours the patient was semiconscious. Thereafter she improved rapidly and by the third day was rational and cooperative. She weighed 174 lb. (79 kg.). At first she was put on a diet that provided 2,550 calories but later on one that furnished 1,500 calories. In four months her weight decreased to 154 lb. (69.9 kg.), and her insulin dose was reduced until none was required. Thus with weight reduction she showed no evidence of diabetes. Five years later, following the regaining of the lost weight, she returned with the characteristic findings of diabetes mellitus. The author has observed repeatedly that obese diabetics achieve normal glucose tolerance curves with loss of weight. At his clinic it has become the practice never to give obese diabetics insulin unless complications make it

advisable. He has seen patients requiring as much as 150 units of insulin daily who have lost all symptoms of diabetes merely by weight reduction. In addition, it has been found that diabetics who remain overweight commonly have diabetic retinitis, renal lesions, and so forth, whereas, those who lost weight and "cured" their diabetes, have remained free from such complications.

Surgery, Gynecology and Obstetrics, Chicago

93:657-782 (Dec.) 1951

- Arteries, Veins, and Arteriovenous Anastomoses in Human Stomach. T. E. Barlow, F. H. Bentley and D. N. Walder.—p. 657.
Neurovascular Mechanism of Mucous Membrane of Stomach. H. B. Benjamin.—p. 672.
Internal Wire-Pin Stabilization for Middle Third Facial Fractures. J. B. Brown, M. P. Fryer and F. McDowell.—p. 676.
*Treatment of Cardiac Arrest: Experimental Study. J. H. Kay.—p. 682.
Mechanism of Electrolyte Imbalance Following Uretersigmoid Transplantation. J. Lapidus.—p. 691.
Ureterocele: Study of 94 Instances in 80 Infants and Children. M. Campbell.—p. 705.
*Cancer Detection Center: Its Effectiveness and Its Role in Control of Cancer, as Determined by a Follow-Up Study of 1,000 Patients. E. E. Clifton and B. Rush Jr.—p. 719.
*Sympathectomy in Treatment of Frostbite. H. B. Shumacker Jr.—p. 727.
Measurement of Pulsatile Arterial Circulation. C. A. Johnson.—p. 735.
Anomalies of First Branchial Cleft. L. T. Byars and R. Anderson.—p. 755.
Adenomamectomy for Benign Breast Lesions. C. O. Rice and J. H. Strickler.—p. 759.
Sex Hormones in Fracture Healing: Experimental Study. W. R. Deaton Jr., F. Forsyth, T. O. Coppedge and H. H. Bradshaw.—p. 763.
Prognosis of Cancer of Cervix by Vaginal Smear: Correlation with Five Year Results. R. M. Graham.—p. 767.

Treatment of Cardiac Arrest.—Cardiac arrest is a surgical emergency that may occur in the form of ventricular standstill or ventricular fibrillation. In ventricular standstill the heart contracts feebly or not at all. In ventricular fibrillation there are incoordinate contractions of individual muscle fibers. In both forms the ventricles are ineffective in expelling blood. The experiments described here were undertaken to determine the most satisfactory methods of treating ventricular standstill and fibrillation. Ventricular standstill and fibrillation were produced 205 times in 72 dogs, and various treatments were employed. Adequate cardiac massage was found to be one of the most important steps in treating ventricular standstill and fibrillation. Ventricular standstill produced by an overdose of ether or chloroform as well as ventricular standstill following the successful electrical defibrillation of hearts in ventricular fibrillation was successfully treated with cardiac massage alone or cardiac massage in conjunction with the injection of various cardiac stimulants. Isopropylphenephrine and barium chloride restored a normal beat to many of the hearts in ventricular standstill. Calcium chloride was a better cardiac stimulant than the former substances, but epinephrine hydrochloride was the best cardiac stimulant. The injection of procaine is not a satisfactory method of treating ventricular fibrillation, even when accompanied by cardiac massage. Cardiac massage for one to two minutes associated with electrical defibrillation was successful in 189 ventricular fibrillation experiments. On only one occasion was it necessary to use procaine as an adjunct to electrical defibrillation. In 29 animals the heart was allowed to fibrillate for from 3 to 62 minutes. The heart was massaged during the entire time and at the end of the allotted time the heart was electrically defibrillated and all of the animals recovered without evidence of neurological changes.

Effectiveness of Cancer Detection Center.—Opinion concerning the effectiveness of cancer detection centers is divided. Initial reports of their results were favorable, but they have been criticised because of: (1) the difficulty in restricting the clinics to asymptomatic patients; (2) the low percentage of detections, (estimated at 1 in 1,000 by some); (3) the high cost per detection; and (4) the large number of patients who do not receive the diagnostic procedures recommended when referred back to their physicians. At the New Haven Cancer Detection Center, established in 1947, more than 3,000 examinations have been conducted. A follow-up study was started in 1950. The routine examination at this center includes history and physical examination, blood count, urinalysis, stool guaiac test, roentgenogram of the chest, Papanicolaou smears of the cervix, and Mazzini

test. Auxiliary services include further diagnostic x-ray studies, endoscopic examinations, and biopsy. A determination of the number of true detections made in 1,000 patients and the number of cancers missed by follow-up of the patients over a period of at least 12 months indicated that most silent cancers were detected by use of all diagnostic facilities and proper follow-up. The percentage of detection may not be high enough to justify the cost of a detection center, but other benefits justify their continuation. These indirect benefits include evaluation of new methods of detection, education of the medical and lay public concerning cancer detection, and early diagnosis of diseases other than cancer. Methods for increasing the yield of cancer detections are discussed, and the authors recommend the use of one of the nonspecific serological tests for cancer in conjunction with the routine cancer detection examination. Patients in whom silent cancers are diagnosed are greatly benefited by the early diagnosis, as indicated by the low incidence of metastatic lesions in these patients.

Sympathectomy in Frostbite.—Sympathetic blocks induced early in the course of frostbite bring about cessation of pain, rapid subsidence of edema, quicker demarcation of viable and gangrenous areas, and more active circulation with better granulations and quicker healing. In this report Shumacker is chiefly concerned with the use of sympathectomy in the later stages of frostbite. He analyzes his experiences with 33 sympathectomies in 20 patients, in all of whom the injury resulted from exposure to dry cold, no cases of trenchfoot or immersion foot being included. In two patients sympathectomy was performed within the first week after freezing, and both patients left the hospital with the wounds healed after 56 and 57 days, respectively. In 10 additional patients sympathectomies were carried out from 2 to 11 months after injury. Twelve lumbar sympathectomies were performed, the procedure being carried out bilaterally in three patients and unilaterally in six; a bilateral dorsal sympathectomy was performed in the 10th patient. All 10 patients had vasoconstriction and sympathetic overactivity even in an ordinary warm environment. Many of them complained of coldness of the feet and hyperhidrosis and cyanosis. Four patients complained of rest pain and in three of the four the pain was burning in character. These symptoms were all relieved after sympathetic denervation except for persistence of very mild pain in one patient. The remaining eight patients were treated for late sequelae of frostbite from 3 to 22 years after the injury. The chief complaints were coldness, numbness, pain, hyperhidrosis, edema, recurrent ulceration, and Raynaud's attacks. Six of these patients had bilateral lumbar sympathectomy, and two had bilateral upper dorsal sympathectomy. The results of sympathectomy were excellent or good in all eight cases.

Texas State Journal of Medicine, Fort Worth

47:799-850 (Dec.) 1951

- Recent Advances in Treatment of Tuberculosis. D. E. Jenkins.—p. 803.
 Pulmonary Decortication. R. R. Ross.—p. 810.
 Fungus Diseases of Lungs: Review of Roentgenologic Manifestations. C. A. Good.—p. 817.
 Pulmonary Adenomatosis and Alveolar Cell Carcinoma. J. P. Abbott.—p. 826.

*Homologous Serum Hepatitis After Transfusions of Blood and Ultraviolet-Irradiated Plasma: Clinical Observations. R. G. Greenlee, R. J. Terrill and J. Q. Sloan.—p. 831.

Serum Hepatitis Following Transfusions.—This report is based on a follow-up study of 1,311 patients who received a total of 2,939 transfusions of whole citrated blood and 77 units of irradiated plasma. Some of these patients received as many as 14 transfusions. Sixteen of the patients died before six months had elapsed and are therefore not included in this inquiry regarding serum hepatitis. A total of 843 patients could be followed up, and among these there were 13 cases of homologous serum hepatitis, 3 of which are regarded as "possible cases," since the patients were not observed during their illness by these authors and their own physicians could not be reached. Ten of the patients received plasma that had been subjected to ultraviolet irradiation; two of them having received no other transfusion beside the irradiated plasma. It is concluded that ultraviolet irradiation probably does not render pooled plasma free from the virus of homologous serum hepatitis.

U. S. Armed Forces Med. J., Washington, D. C.

2:1593-1778 (Nov.) 1951. Partial Index

- Goiter Heart. S. H. Rosen.—p. 1593.
 *Treatment of Nerve-Gas Casualties. J. R. Wood, P. F. Dickens Jr., J. Rizzolo and M. W. Bayliss.—p. 1609.
 Evolution of Medical Air Transport Policies. J. A. Baird.—p. 1619.
 Medical Experiences in Korea. D. E. Carle.—p. 1623.
 Chemosurgery. G. H. Ekblad.—p. 1631.
 Proper Use of Outpatient Clinic. W. F. Bowers.—p. 1641.
 Lymphogenous Cysts of Mediastinum: Cystic Hygromas, Pericardial Cysts, and Pericardial Diverticulum. R. B. Brown and R. G. Dunn.—p. 1651.
 Multiple Eosinophilic Granuloma of Bone with Pulmonary Involvement. A. J. Brody and J. O. Gillespie.—p. 1669.
 Eosinophilic Granuloma of Rib. S. W. French III.—p. 1681.
 Regional Enteritis. D. R. Sewell and J. H. Wilkins.—p. 1685.
 Management of Neurogenic Bladder. J. C. Kimbrough.—p. 1691.
 *Vivax Malaria with Long Incubation Periods: Report of Seven Cases. E. E. Eddleman Jr., W. H. Hale and W. M. Snowden.—p. 1693.
 Present Concepts of Compensation for Fluid and Electrolyte Alteration. S. H. Walker.—p. 1699.
 Presacral Neurofibroma. G. Alvary.—p. 1709.
 Clinical Effects of Delta 5 Pregnenolone in Rheumatoid Arthritis. A. R. Higgins, R. E. Jones Jr. and T. W. D. Smith.—p. 1717.
 Symmetrical Serous Synovitis. R. G. Thompson and C. Z. Berry.—p. 1723.
 Cervical Spine Radiography. R. W. Augustine and R. W. Eells.—p. 1729.
 Primary Split-Skin Graft in Treatment of Pilonidal Cysts.—p. 1733.

Treatment of Nerve Gas Casualties.—The nerve gases are a group of highly toxic chemical agents. Like the newer insecticides such as "parathion," the nerve gases depress the cholinesterase activity of the tissues below a functional threshold. The manifestations of acute poisoning by these agents resemble those produced by excessive stimulation of the parasympathetic nervous system, the central nervous system, and somatic motor nerves. Therefore, these substances should be classified as cholinergic agents. The nerve gases are readily absorbed from the skin, mucous membranes, respiratory tract, and the gastrointestinal tract. The signs and symptoms of poisoning by these agents include muscarine-like, nicotine-like, and central nervous system effects. They include anorexia, nausea, vomiting, abdominal cramps, tenesmus, and diarrhea. There is increased sweating, lacrimation, and tightness of the chest, with prolonged wheezing expiration suggestive of bronchoconstriction. The pupils become constricted and occasionally are unequal in size. There is increased fatigability associated with muscular weakness and twitching. The central nervous system effects include giddiness, insomnia, tension, anxiety, depression, and changes in the electroencephalogram. There is a fairly narrow margin between the dose of the nerve gas that produces systemic symptoms and the dose that would probably be lethal. The treatment of anticholinesterase poisoning is based on blocking the effects of accumulated acetylcholine by giving atropine and appropriate symptomatic therapy. The following lifesaving and therapeutic measures are mentioned: (1) termination of exposure, masking, and removal from the contaminated area, and decontaminating the skin surfaces by removal of contaminated clothing and equipment; (2) administration of atropine as soon as possible after poisoning and repeating it as necessary; (3) administration of artificial respiration to paralyzed persons. Symptomatic treatment may include the use of trimethadione or thiopental sodium to control convulsions not controlled by atropine, pentobarbital as a sedative to allay apprehension, and atropine or homatropine to overcome miosis.

Vivax Malaria with Long Incubation Periods.—Seven proved cases of vivax malaria seen at an infirmary from May through July, 1951, in military personnel returned from Korea are reported. These cases are of special interest because the symptoms of malaria occurred from 2½ to 8 months after their return to the United States. All were successfully treated with chloroquine.

Wisconsin Medical Journal, Madison

50:1157-1332 (Dec.) 1951

- Some Psychiatric Implications of Gynecologic Surgery. C. L. Kline.—p. 1178.
 Chemical Peritonitis from Oxycel: Case Report. G. A. Fostvedt and L. M. R. Fostvedt.—p. 1183.
 Further Experience with Rebreathing Heart Test. A. A. Holbrook.—p. 1185.
 Constructive Values in Training of Slow Learning Children. L. Kanner.—p. 1191.

FOREIGN

Ann. Chirurgiae et Gynaecologiae Fenniae, Helsinki

40:135-202 (No. 3) 1951. Partial Index

- *Cholecystitis and Cholelithiasis in Childhood. R. Wilenius.—p. 135.
 Gynecologic Tumors Extending to or Above Umbilicus. O. Kinnunen and M. Kauppinen.—p. 147.
 Microscopic Examination of Placenta in Normal, Premature, and Post-mature Births, and in Gestosis. H. Sauramo.—p. 164.
 Sexual Function in Women After Irradiation for Cervical Carcinoma. V. Kahanpää and T. Gylling.—p. 189.
 Acute Intestinal Obstruction as Result of Cancer of Colon. E. Puranen.—p. 194.

Cholecystitis and Cholelithiasis in Childhood.—In school children the symptoms of cholecystitis and gallstones are fairly similar to those in adults, but in infants the diagnosis of cholecystitis is difficult since the symptoms are lack of appetite, vomiting, and diarrhea with or without fever. Most observers agree that the prognosis for acute cholecystitis in childhood is poor unless the patient is subjected to early operation. Cholecystitis following typhoid fever seems to be particularly malignant if mixed infection occurs. Wilenius presents five case reports. In case 1 the etiology was not clear, but typhoid gastroenteritis was suspected, and perforation and diffuse peritonitis occurred. The diagnosis was made post mortem. In case 2 acute cholecystitis may have been caused by measles. A swelling was palpable between the umbilicus and right costal margin that proved at operation to be an inflamed gallbladder. Cholecystostomy was performed, and the patient recovered, but later repeated attacks of pain occurred. In case 3 acute typhoid cholecystitis was suspected; cholecystectomy was performed and the patient recovered. In case 4 acute pneumococcal cholecystitis was cured by cholecystectomy. The symptoms of gangrenous cholecystitis in case 5 resembled those of appendicitis; cholecystectomy was successful. In none of these patients were gallstones found. The author also studied autopsy records of 2,049 persons less than 19 years of age. Concrements in the gallbladder were found in 0.33% of the cases. The gallstones were evidently asymptomatic in all these cases.

Beiträge zur klinischen Chirurgie, Munich

183:257-384 (No. 3) 1951. Partial Index

- Intestinal Obstruction After Laparotomy. R. Stich.—p. 259.
 Late Functional Results of Unilateral Pelvic Resection Performed During Period of Growth. E. Heller.—p. 265.
 Perirenal Hemangioma as Cause of Recurrent Perirenal Hematoma. P. Scheid.—p. 270.
 Occurrence of Pancreatic Injuries After Gastrectomy and Their Sequelae. E. Lidas.—p. 287.
 *Conservative Treatment of Prolapsed Posterior Intervertebral Lumbar Disk, with Particular Consideration of Presacral Procaine Hydrochloride Infiltration According to Pendl and Heile's Paravertebral Anesthesia. K. Schulte.—p. 325.

Conservative Treatment of Prolapsed Intervertebral Disk.

Twenty-eight patients with prolapsed posterior intervertebral disk were given 46 presacral and 54 bilateral paravertebral infiltrations of anesthetics; some patients were given up to three treatments at intervals of several days. In 22 cases 32 presacral infiltrations of 150 cc. of 0.25% solution of procaine hydrochloride and 38 bilateral paravertebral infiltrations of 50 cc. of 0.25% solution of procaine hydrochloride were given; in 9 cases 16 presacral and 16 bilateral paravertebral infiltrations of a 0.05% solution of 2(N-piperidyl)ethyl *p*-propoxyphenyl ketone hydrochloride ("falikain") were given. In three of the nine cases "falikain" was substituted for the previously used procaine hydrochloride. In special cases the anesthesia was combined with extension by Glisson's sling, traction applied on the legs by weight, and application of a trunk plaster cast. Treatment has not yet been terminated in 5 of the 28 patients; of the remaining 23, 5 were lost to observation and 18 were subjected to follow up examinations. Of these 18 patients, good results were obtained in 14 and satisfactory results in 4. The method thus was successful in about 90% of the patients. In two instances undesirable effects of the treatment were observed, consisting of vomiting, headache, and small pulse in one patient, and of severe collapse in the other. This second patient was unconscious for one hour and had no pulse, since in the course of the paravertebral infil-

tration the anesthetic solution apparently had entered the dural sac. Consequently patients should be admitted to the hospital for the anesthesia. Conservative treatment of prolapsed intervertebral disk should first be given a trial in every instance, since not only lumbar pain and sciatica may be improved but also scoliotic and kyphotic pain. Surgical treatment should be limited to patients with definite indications.

Biochemical Journal, London

50:1-144 (Nov.) 1951. Partial Index

- Precise Determination of Haemoglobin in Blood by Abridged Photoelectric Spectrophotometry. J. W. Nicholas.—p. 1.
 Activation of Proteolytic Enzyme in Blood by Animal Tissue. T. Astrup.—p. 5.
 Electrical Stimulation in Vitro of Metabolism of Glucose by Mammalian Cerebral Cortex. H. McIlwain, G. Anguiano and J. D. Cheshire.—p. 12.
 Assimilation of Amino-Acids by Bacteria. Effect of Certain Amino-Acids on Accumulation of Free Glutamic Acid by *Staphylococcus Aureus*: Extracellular Peptide Formation. E. F. Gale and M. B. Van Halteren.—p. 34.
 Enzymes Concerned in Synthesis of Glycogen from Glucose in Brown Adipose Tissue. N. H. Creasey and C. H. Gray.—p. 74.
 Role of Gastric Urease in Acid Secretion. R. E. Davies and H. L. Kornberg.—p. 119.
 Specificity of Cobra-Venom Cholinesterase. L. A. Mounter.—p. 122.

British Journal of Radiology, London

24:637-692 (Dec.) 1951

- Orbital X-Ray Therapy of Progressive Exophthalmos. A. Jones.—p. 637.
 Digital Markings in Radiographs of Skull in Children. D. Macaulay.—p. 647.
 Simplified Method of Pelvimetry Using "Pelvimetry Protractor." G. Doel.—p. 653.
 Pyloro-Duodenal Spasm: Its Relaxation with Procaine. P. Cave.—p. 659.
 Physical Measurements on 2 MeV. X-Ray Generator. J. L. Howarth, J. C. Jones and H. Miller.—p. 665.
 Design of Wedge Filters for X-Ray Therapy. A. C. Groom.—p. 676.
 Uptake of Tritium-Labelled Water Vapour by Mammalian Lung. I. G. Campbell, D. F. White and P. R. Payne.—p. 682.

British Medical Journal, London

2:1415-1474 (Dec. 15) 1951

- Anaemia of Pregnancy Among Africans in Nigeria. A. W. Woodruff.—p. 1415.
 *Investigation of Salt and Water Balance in Migraine. D. A. Campbell, K. M. Hay and E. M. Tonks.—p. 1424.
 Deafness as an Epidemic Disease in Australia: Note on Census and Institutional Data. H. O. Lancaster.—p. 1429.
 Graves's Disease: Clinical Types and Their Management. F. F. Rundle.—p. 1433.
 Note on Mantoux Sensitivity in Sick Children. C. Ounsted and V. Smallpeice.—p. 1437.
 Case of Moniliasis. F. C. Ormerod and I. Friedmann.—p. 1439.
 Primary Hyperparathyroidism (Adenoma) Simulating Sarcoidosis: Report of Case. H. W. Salmon and G. G. Meynell.—p. 1440.
 Monocytic Leukaemia and Pulmonary Tuberculosis Complicating Pregnancy. G. Beven.—p. 1442.

Salt and Water Balance in Migraine.—Campbell and associates suppose that the cerebral swelling occurring in migraine is part of a generalized edema that is known to occur before and during the early part of an attack of migraine. In more than 200 cases they observed edema of various parts of the body before an attack. Women often volunteer the information that their skirts become tight or their legs swell, while a number of subjects notice an increase in body weight. It is also known that diuresis may occur in the terminal phase of an attack of migraine. One of the authors administered 7.5 gm. of urea twice daily over a period of at least two months. A definite alleviation of symptoms was reported in 51 of 66 cases, a much better result than has been obtained by other forms of medication. Since the main action of urea is diuretic, these clinical findings seem to indicate that diuresis is a physiological means of restoring the body fluids to their normal balance. The salt and water metabolism of patients with migraine was therefore studied by means of a water imbibition test and by analysis of the blood and urine during the migraine cycle. In the premigraine phase, particularly in the early stages of the attack itself, the blood sodium rises to a high level, while at the same time there is marked hydration of the blood. The excessive secretion of sodium and chloride that follows a water imbibition test suggests that abnormal sodium metabolism is present almost continuously. The suggestion is

made that these disturbances are due to dysfunction of the hormones governing salt and water metabolism of the adrenal cortex and posterior pituitary gland, and that in women they are exacerbated by the influence of certain sex hormones.

Bullettino delle Scienze Mediche, Bologna

123:267-386 (July-Sept.) 1951. Partial Index

- Methods of Cancer Cytodiagnosis and Their Limited Use. G. Montaldo.—p. 267.
 Scars, Limits, and Method of Intravenous Administration of Iron. F. Scarlioni.—p. 277.
 Studies on Cellular Protein Metabolism: Influence of Colchicine on Structure and Cytochemistry of Serous Cells. A. Milletti.—p. 288.
 *General Adaptation Syndrome in Tuberculous Infection. L. Matteucci.—p. 292.

General Adaptation Syndrome in Tuberculous Infection.—According to Selye's concept of the general adaptation syndrome, tuberculous infection is a manifestation of the organism's reaction to the presence of Myco. tuberculosis. In its first contact with the organism the bacterium causes a specific stimulus to which the organism reacts by forming antibodies, and a non-specific stimulus, the "stressor," to which the organism reacts with the hormonal mechanism described by Selye. The anterior hypophysis secretes corticotropin (ACTH) that stimulates adrenocortical production of mineralocorticoids and glucocorticoids. In primary tuberculous infection in a child, all three stages of the general adaptation syndrome may be seen. The preallergic phase characterized by negative reactions to tuberculin tests represents the alarm reaction period during which the organism has not been able to adapt itself to the new condition. A stage of resistance follows during which adaptation reaches its maximum. In some organisms, despite prolonged resistance, Myco. tuberculosis does not find an adequate opposition, and the stage of exhaustion occurs. Sometimes the first tuberculous infection is followed by primary tuberculous bronchopneumonia, primary caseous pneumonia, or extrapulmonary dissemination through the blood; this represents the period of "maladaptation" that may be attributed to imbalance between mineralocorticoids and glucocorticoids. The phase of resistance lasts as long as the anterior hypophysis secretes corticotropin in quantities sufficient to stimulate and maintain adrenal cortex production of mineralocorticoids and glucocorticoids in optimal proportion. The mineralocorticoids have a stimulating effect on tissues, cause exudative or allergic reactions, and stimulate liberation of histamine that enhances the virulence of Myco. tuberculosis. The lung contains more histamine than any other organ. If the bacterium is present when the action of mineralocorticoids is not balanced by the histamine-inhibiting action of glucocorticoids, its virulence is greatly increased, and allergic or exudative phenomena are manifested. The author gave 6 mg. of corticotropin every 24 hours for 18 days to a 3-year-old child with apical tuberculosis, and 6 mg. every 12 hours for 15 to 20 days to two 6-year-old children with adenopathy of the hilus. The exudative processes regressed, thus proving that the tuberculous infection developed when, for want of corticotropin secretion, the balance between mineralocorticoids and glucocorticoids was altered.

Deutsche Zeitschrift für Nervenheilkunde, Berlin

166:177-272 (No. 3) 1951. Partial Index

- Surgical Observations on Sympathetic Innervation of Pelvic Organs, Particularly of Anal Sphincter. O. Goetze.—p. 177.
 *Trigeminal Neuralgia and Arterial Hypertension. G. Döring and R. Magun.—p. 196.
 Animal Experiments on Dissemination of Electric Excitation: I. Characteristics of Different Parts of Cortex and Mutual Modification of Several Simultaneously Induced Foci. R. Janzen, R. Magun and F. Becher.—p. 223.
 Cerebrospinal Fluid Cells Under the Phase Contrast Microscope. F. Junker.—p. 237.
 Determination of Potassium in Cerebrospinal Fluid. H. Rodeck.—p. 268.

Trigeminal Neuralgia and Arterial Hypertension.—The examination of 118 patients with trigeminal neuralgia revealed that they had hypertension. Döring and Magun regard the arterial hypertension as the basic disease, pointing out that neuralgic paresthesia (Bernhardt's paresthesia) is also observed in a high percentage of patients with hypertension. They assume that the basic hypertensive process produces tissue changes in the gasserian ganglion

that in turn cause the neuralgia. The tissue changes may also, however, be produced by other disorders. Trigeminal neuralgia is not a "vasoneurosis" or a "vasomotor crisis." Physiologically it can be regarded as a "short circuit" between the transmission of the pressure and pain perceptions. Clinical observations do not justify the concept that vascular spasms are responsible for the typical pain attack. The anatomic cause of the "short circuit" is probably located in the gasserian ganglion; more particularly it is believed that the hypertrophy of the covering syncytium with increase in the basket-like bundles and proliferation of the amphicytes might explain the interruption.

Journal of Bone and Joint Surgery, London

33B:493-668 (Nov.) 1951. Partial Index

- Late Results of Arthrodesis of Foot. A. J. Drew.—p. 496.
 Pan-Arthrodesis for Paralytic Flail Foot. M. Bastos Ansart.—p. 503.
 Treatment of Trochanteric Fractures. J. C. Scott.—p. 508.
 Trochanteric Fractures of Femur: Review of 80 Cases with Description of "Low-Nail" Method of Internal Fixation. R. H. V. Hafner.—p. 513.
 *Tuberculosis of Spine: Analysis of Results of Conservative Treatment and Factors Influencing Prognosis. J. Dobson.—p. 517.
 Osteoarthritis of Pisiform-Triquetral Joint: Report of Three Cases. S. A. Jenkins.—p. 532.
 Dangerous Type of Fracture of Foot. W. Gissane.—p. 535.
 Treatment of Claw Toes by Multiple Transfers of Flexor into Extensor Tendons. R. G. Taylor.—p. 539.
 Fractures of Radius and Ulna. E. M. Evans.—p. 548.
 *Congenital Dislocation of Hip. G. L. Burke.—p. 562.
 Complication of Lateral Meniscectomy. T. J. Fairbank and E. S. Jamieson.—p. 567.
 Calcinoses. A. R. Hamilton.—p. 572.
 Syphilitic Disease of Long Bones in the Bantu. S. Skapinker and DeV. Minnaar.—p. 578.
 Chronic Bone Infections in Africans: 10 Cases from Nigeria. T. L. Lawson.—p. 584.
 Myositis Ossificans Complicating Anterior Poliomyelitis. F. V. Costello and A. Brown.—p. 594.
 Pectoralis Major Transplant with Arthrodesis of Shoulder in Case of Injury to Upper Trunk of Brachial Plexus. K. S. Grewal and Iqbal Singh.—p. 598.
 Traumatic Anterior Dislocation of Hip. R. S. Henderson.—p. 602.
 Unusual Lesion of Ulnar Nerve. F. C. Dwyer.—p. 604.

Tuberculosis of the Spine.—Tuberculosis of the spine in 914 patients was treated almost entirely by conservative measures; the cervical spine was involved in 32 (3.5%), the thoracic spine in 394 (43.1%), the lumbar spine in 301 (32.9%), the thoracolumbar spine in 153 (16.7%), and the lumbosacral articulation in 34 (3.8%). Of the 914 patients, 443 had other active tuberculous foci in the body (multiple lesions) and 471 had no other foci. Of the 914 patients, 171 died, a mortality rate of 18.7%; of the 443 patients, 113 died, a mortality rate of 25.5%; and of the 471 patients, 58 died, a mortality rate of 12.3%. Chronic secondary infection was present in abscesses and sinuses in 508 patients, and 97 (19.1%) of them died. Of 165 patients with paraplegia, 41 (24.8%) died. To determine late results three years after discharge from hospital, the working capacity of 390 patients was ascertained; 335 (86%) had full working capacity, 23 (5.8%) had partial capacity, and 32 (8.2%) could not work. The ill effect of complications on the prognosis is emphasized, particularly in cases of multiple foci of active tuberculosis, secondarily infected abscesses and sinuses, and paraplegia. The incidence of paraplegia was highest in the patients with thoracic disease, occurring in 31.2% of them. An attempt was made to determine the site of the primary bone focus from the radiographic changes. Early epiphyseal changes were present in 302 patients (33%); the central focus originated in the spongy tissue of a vertebral body in only 106 patients (11.6%); subperiosteal lesions were present in only 19 patients (2.1%); and the neural arch was the site of the primary infection in only 4 patients (0.5%). In 483 patients (52.8%) widespread destruction had taken place when the patient first came under observation. Healing of the spine by spontaneous bony fusion of the affected vertebral bodies occurred in 184 patients (27.3%), and apparently sound fibrous fusion occurred in 489 patients (72.7%). Of the 184 patients, 27 (14.6%) required further hospital treatment, 5 because of reactivation of the disease, 7 because of persistent infection in the sinuses, 2 with paraplegia, 3 with a new focus in the spine, and 10 because of extraspinal foci. Of the 489 patients, 110 (22.5%) required further treatment, 47 because of reactivation, 12 with persistent sinuses, 15 with increasing deformity, 8 with paraplegia, 5 with new foci in the spine, and 23 with extraspinal foci.

Congenital Dislocation of the Hip.—According to a new concept of the etiology of congenital dislocation of the hip, increasing deformity is the result of soft tissue contracture (or a relative shortening of normal muscle) upon which growth of bone is superimposed. Thus the process is a simple accident to a normal fetus. It is suggested that the adductor muscles, assisted by the flexors, provide the principal dislocating force and these constitute the "soft tissue contracture." A spurt of growth by the femur is the "superimposed growth." In the fetal position the femoral head is forced against, and over, the posteroinferior rim of the acetabulum, which at the time of dislocation is about the shape and size of a vest button, and too small for the femoral head. A slight discrepancy in growth between muscle and bone therefore results in deformity. If the hips are reduced, reduction maintained, and a wide range of movement of the hips allowed, the result should be a normal hip. Contact and function are mandatory for the normal development of the hip. Early diagnosis is important and should be made at birth. A mobile brace is described that allows a wide range of movement while safely maintaining reduction. A case is reported in which treatment according to this method was instituted on the third day after birth. The success of this method of treatment supports the conception of the etiology on which it is based.

Lancet, London

2:1097-1148 (Dec. 15) 1951

Infection and Resistance in Young Animals. R. Lovell.—p. 1097.

*Shunting in Human Kidney. S. N. De and K. P. Sengupta.—p. 1100.

Clinal, Social, and Occupational Aspects of Industrial Dermatitis.

M. Hewitt.—p. 1105.

Charcot Joints in Diabetic Neuropathy. J. Lister and R. H. Maudsley.

—p. 1110.

Effect of A.C.T.H. on Erythrocyte-Sedimentation Rate and Plasma-

Fibrinogen and Serum-Protein Levels in Normal Persons. G. R.

Fearnley and J. J. Bunim.—p. 1113.

Paroxysmal Tachycardia in Infancy. A. W. B. Edmunds.—p. 1116.

*Tromexan Therapy: Dosage and Indications. C. Hougic.—p. 1118.

Shunting in Human Kidney.—The possibility that blood is diverted from the renal cortex to the renal medulla was conceived by Macgrath and Findlay in their study of the kidney in black-water fever. Later, this hypothesis was evoked as the basic causal factor in various clinical conditions characterized by oliguria and/or anuria, azotemia, and tubular degeneration. The anatomic evidence was, however, limited to reports of gross pallor of the cortex and deep congestion of the medulla, with degeneration of parts of the tubules chiefly situated in the cortex. Radiographic and gross anatomic evidence of such corticomedullary diversion of the renal blood flow after experimental stimulation of various nerves in laboratory animals was adduced by Trueta and associates, who regarded their experimental observations as evidence that such differential adjustment of intrarenal blood flow occurs in various pathological conditions in man. Other investigators, however, doubted this concept of corticomedullary diversion of blood in human kidneys, since none of the methods used to demonstrate this shunting in the living animal seemed applicable to man. To obtain more definite anatomic evidence of corticomedullary diversion of blood in man, De and Sengupta studied macroscopically and by means of Pickworth's stain thick frozen sections of kidneys collected at necropsy. The pathological conditions in patients whose kidneys were examined included burns, cholera, copper sulfate poisoning, acute hemorrhage, eclampsia, and asphyxia. None of the patients had survived for more than 72 hours from the onset of their illness. In all these conditions there was evidence of shunting of the renal blood from the cortex to the medulla, usually through the juxtamedullary glomeruli, but in extreme cases the blood from the arcuate vessels entered the medulla directly through the true vasa recta. The juxtamedullary glomeruli and their efferent vessels in man do not seem to supply blood to the tubules in the boundary zones of the cortex and of the medulla, which receive their supply from higher glomeruli. Damage to the parenchyma in the cortex and in the lower part of the medulla can generally be correlated with the degree and duration of ischemia in these areas. The damage includes cloudy swelling, fatty change, and necrosis of the tubular epithelium. The collecting tubules seem to be relatively more resistant than the convoluted tubules and their limbs, but no evidence was found of selective damage to the distal tubules as opposed to the proximal ones.

Ethyl Biscoumacetate Therapy.—In 1949 ethyl biscoumacetate (tromexan®), or bis-3:3'-(4-oxycoumarinyl) ethyl acetate, became available for clinical trial. This anticoagulant is absorbed and excreted more rapidly than bishydroxycoumarin. Hougic used ethyl biscoumacetate in 50 cases. They included 22 of coronary thrombosis, treated for an average period of 28 days; 15 of post-operative thrombophlebitis and phlebothrombosis, treated for an average of eight days; 9 of postoperative pulmonary embolism, with and without manifestations in the leg, treated for an average of 14 days; 3 of nonsurgical thrombophlebitis and phlebothrombosis, treated for an average of 14 days; and 1 of thrombophlebitis migrans. In 44 patients the results were excellent, 3 had thromboembolic recurrences but progressed satisfactorily, and 3 died of coronary thrombosis, one within four days of admission. It was found most satisfactory to give initially 600 mg. followed by 300 mg. every six hours. Further dosage was based on the prothrombin concentration produced by the previous day's amount, assuming that the action of the drug is maximal 24 hours after its administration and that one day's dosage is excreted almost entirely during the subsequent day. The prothrombin concentration is best maintained at 15%, so that if the patient becomes resistant or sensitive to the drug, the dose can be increased or diminished before the prothrombin rises above 20% or falls below 10%. In most patients the prothrombin level is stabilized in a few days on 300 to 600 mg. daily. The importance of maintaining the prothrombin concentration below 20% is emphasized and illustrated by three cases in which thromboembolic incidents occurred when the prothrombin concentration was between 20% and 30%. Since tolerance and increased sensitivity to ethyl biscoumacetate may develop very quickly, the prothrombin concentration should be estimated at least every 48 hours. It is contraindicated when there is a recent operation wound that may bleed or a recent history of peptic ulcer; in patients who may need surgery at short notice, and where intestinal absorption is impaired or there is recurrent vomiting. In any of these circumstances heparin is the best anticoagulant. In all other cases ethyl biscoumacetate should be given following administration of heparin.

Medical Journal of Australia, Sydney

2:657-688 (Nov. 17) 1951

Nocturnal Symptoms. C. Engel.—p. 657.

Recurrent Pterygium. J. B. G. Gibson.—p. 664.

Macrocytic Anaemia of Pregnancy. D. F. Lawson and J. H. Bolton.—p. 669.

The Doctor in Court. J. Bostock and A. H. Robertson.—p. 671.

Case of Toadfish Poisoning. C. Duncan.—p. 673.

2:689-724 (Nov. 24) 1951. Partial Index

Present-Day Problems of Prefrontal Leucotomy and Its Varieties. O. Schmalzbach.—p. 689.

Acute Accidental Poisoning in Children: Its Incidence, Diagnosis and Treatment. D. C. Ryan.—p. 702.

Bengal Rose as Aid in Diagnosis of "Kerato-Conjunctivitis Sicca" (Sjögren's Syndrome). K. O'Day.—p. 702.

Note on Use of Antibiotics in Treatment of Infections with Some Gram-Negative Bacilli. S. V. Keating.—p. 709.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

95:3301-3364 (Nov. 10) 1951. Partial Index

*Treatment of Liver Abscess with Chloroquine. J. J. C. P. A. Roovers and P. B. van Steenis.—p. 3316.

Retraction Syndrome: Little Known Manifestation of Defect of External Rectus Muscle. A. M. Hamoen.—p. 3334.

Chloroquine in Liver Abscess.—Roovers and van Steenis discuss the various drugs that have been used in the treatment of liver abscess and amebiasis, pointing out that liver abscess is practically always a complication of intestinal amebiasis. The therapeutic efficacy of a drug depends on its amebicidal power and on its concentration where amebas are found, that is, in the intestinal wall and liver in the histolytic form, and in the intestinal lumen in the minuta forms. The authors describe four patients in whom chloroquine proved highly effective, the effect being both rapid and lasting. No relapse had occurred up to two years after treatment. Two of the patients who responded to chloroquine had become refractory to emetine. Like emetine treatment, the chloroquine treatment of hepatic abscess should be followed by a course of treatment with chiniofon or carbarsone, in order to kill the minuta forms of the amebas in the intestinal lumen.

Nordisk Medicin, Stockholm

46:1553-1590 (Oct. 17) 1951. Partial Index

Rönnskär Disease (Industrial Disease in Employees of Rönnskär Smelting Works). K. D. Lundgren, N. O. Richtner and T. Sjöstrand.—p. 1556.
Xylocaine in Conduction Anesthesia. A. J. Bowden Jr., J. G. Riley and R. A. Hingson.—p. 1562.

*Hexamethonium Bromide in Hypertension. I. Persson.—p. 1564.

*Succinylcholine Iodide as Muscle Relaxant in Electroshock Treatment. G. Holmberg and S. Thesleff.—p. 1567.

Serum Iron in Endogenous Mental Depression Before and After Electroshock Treatment. B. Rönson Källström.—p. 1570.

Effects of Accidental Arterial Injection. F. Truelsen.—p. 1571.

Glandular Form of Toxoplasmosis in Child. A. Landau.—p. 1575.

Hexamethonium Bromide in Hypertension.—Persson believes treatment with hexamethonium bromide to be specially indicated when ophthalmoscopy shows only hypertensive changes without arteriosclerosis. In six such patients dosage up to 4 gm. daily was quickly reached, and in some cases the dose could be reduced about half after several weeks without rise in blood pressure. In young patients with hypertension considerable improvement also appeared in the subjective symptoms. In patients in whom ophthalmoscopy revealed hypertension together with arteriosclerosis there was a minor reduction in the blood pressure on treatment with hexamethonium bromide, and the subjective symptoms abated only slightly. In these patients smaller doses were given, to avoid distressing side effects. In 10 patients the treatment resulted in a pronounced fall in the systolic blood pressure.

Succinylcholine Iodide as Muscle Relaxant in Electroshock Treatment.—Holmberg and Thesleff applied succinylcholine iodide, shown to have a brief relaxing effect of from one to 10 minutes, depending on the dosage, without toxic effects, to produce muscle relaxation in electroshock. They find its rapid, powerful, and brief effect ideal. Combined with a rapidly acting barbiturate, succinylcholine has been administered intravenously in 108 patients since early 1951, with a total of 439 shock treatments. The diagnosis was usually depression, mild schizophrenia, and in some cases psychoneurosis. No serious complications occurred during the treatment.

Philippine Medical Association Journal, Manila

27:591-638 (Oct.) 1951

Agricultural Control of Malaria. A. Ejercito.—p. 591.

Cysts of Pancreas: Report of Two Cases. A. G. Sison, C. Lazatin, P. C. Campos and R. Apostol.—p. 608.

Surgical Aspects of Breast. J. Estrada and P. T. Nery.—p. 613.

Brief Bibliography of Leprosy in the Philippines. A. Y. Argosino.—p. 617.

Presse Médicale, Paris

59:1631-1650 (Dec. 8) 1951

*Autonomous Miliary Tuberculosis of the Liver (Pylephleogenous Hepatic Granulitis with Primary Course). M. Janbon and L. Bertrand.—p. 1631.
Fatal Subacute Encephalitis with Involuntary Unilateral Rhythmic Movements Associated with Simultaneous Loss of Consciousness: Report of an Anatomicoclinical Case. J. A. Chavany, G. Guiot and D. Hagenmüller.—p. 1632.

Miliary Tuberculosis of the Liver.—The occurrence of autonomous miliary tuberculosis of the liver is reported in two women, aged 28 and 29. The disease was characterized by indolent enlargement of the liver associated with rise of temperature and malaise; there were no hypertrophy of the spleen and no signs or symptoms of enteritis. Roentgenograms of the chest revealed no pulmonary miliary lesions. Puncture biopsies of the liver revealed great density of miliary tubercles in the liver, particularly in the portal canals; some of the lesions were caseous. The pylephleogenous origin from latent tuberculosis of the mesenteric lymph nodes with fistulization into a branch of the portal vein seemed very likely. Animal experiments performed more than 50 years ago in which tubercle bacilli were injected into the mesenteric vein suggested the possibility of autonomous hepatic miliary tuberculosis that now has been demonstrated by liver biopsy in these cases. Complete recovery resulted from treatment with 1.5 gm. of streptomycin daily for eight months in one patient, and from treatment with 1 gm. of streptomycin daily by intramuscular route combined first with 1 gm. of streptomycin orally and later with 12 gm. of *p*-amino-

salicylic acid daily for seven months in the other patient. During treatment, repeated liver biopsies revealed more or less rapid cicatrization of the lesions or their disappearance between the seventh and eighth month of the treatment.

Revista Clínica Española, Madrid

42:301-368 (Sept. 15) 1951. Partial Index

*Roentgenographic Visualization of Aqueduct and Third and Fourth Ventricles in Hydrocephalus. S. Obrador, M. Arrazola and J. Sánchez Juan.—p. 309.

Influenza and Other Virus Diseases: Pathogenesis of Virus Diseases. J. Carreras Pico.—p. 311.

Intestinal Volvulus: Comments and Case Reports. E. Santo-Tomás Cobos.—p. 318.

Clinical Aspects of Hepatargy: Importance of Changes in Enzymatic Functions of Liver. V. López Montero.—p. 322.

Action of Antibiotics and of Chemotherapeutic Substances in Acute Abdominal Disorders. A. Pascual y Megías.—p. 329.

Glossitis Cured by Folic Acid: Glossopathy from Folic Acid Deficiency? A. Casas Carnicero.—p. 331.

Roentgenographic Visualization of Ventricular System.—A satisfactory technique for roentgenographic visualization of the third and fourth ventricles and the aqueductus cerebri in infants and children with hydrocephalus was recently described by Ziedses des Plantes. With the patient on his back, 10 or 20 cc. of air is injected into the third ventricle, either through the fontanel (in infants) or through a hole made by trephination (in children). The head of the patient is slowly rotated on the table lifting the patient by the feet, first to an oblique and then to a vertical posture. One roentgenogram is made for each rotation of the head. The air enters the third ventricle. If there is no obstruction, air passes as the head rotates to the posterior part of the third ventricle, the aqueductus cerebri, the fourth ventricle, and the basal cisterns. Obstruction at a given point of the ventricular system is shown in the roentgenogram. The technique is of value in visualizing obstruction as cause of hydrocephalus in infants and children and in planning proper operation. Three cases are reported in a child 10 years old and 2 infants, 2 and 17 months old, respectively. Obstructions due to stricture of the aqueductus cerebri in two cases and to imperforation of the Luschka and Magendie foramina in one case were demonstrated by this technique. The procedure was well tolerated by infants and children.

Revista Médica de Costa Rica, San José

18:169-192 (Aug.) 1951

New Orientations in Treatment of Myxedema with Myocardial Infarct. G. Deltour and I. Benzecry.—p. 172.

False Giant Diverticulum and Gastric Carcinoma: Survival for 5½ Years. J. Berrocal, E. López, R. Céspedes and others.—p. 181.

*Rapid Technic for Anatomicopathologic Diagnosis of Yellow Fever. R. Céspedes Fonseca.—p. 186.

Rapid Pathologic Diagnosis of Yellow Fever.—An outbreak of yellow fever recently occurred in three provinces in Costa Rica. The number of cases was large and the death rate was very high. During this outbreak a new technique for a rapid accurate pathologic diagnosis of yellow fever was tested at more than 40 necropsies. Liver smears are used, which are fixed for five minutes in a 10% formaldehyde ("formalin") solution, absolute alcohol or alcohol-ether and then stained with hematoxylin eosin. The presence of Councilman bodies in the stained smears is absolute proof of yellow fever. Best results are obtained when the smears are taken from bodies of persons dying in the acute stage of yellow fever. False negatives may occur in cases in which death occurs more than 10 days after the onset of the disease.

Semaine des Hôpitaux de Paris

27:3457-3502 (Nov. 26) 1951. Partial Index

*Pyruvic Acid Metabolism in Diabetes Mellitus. H. Lestrade.—p. 3457.

*Treatment of Severe Acidosis in Patients With Diabetes Mellitus (Ketosis, Acidosis and Coma); Personal Records with Results. E. Azerad and J. Nataf.—p. 3463.

Pyruvic Acid Metabolism in Diabetes Mellitus.—The blood of 15 patients with diabetes mellitus in the absence of ketosis contained almost normal amounts of pyruvic acid (10 mg. per liter on the average). The pyruvic acid content of the blood was

increased from 10 mg. per liter to 21 mg. per liter by relatively moderate muscular exertion in one of the author's patients. Simultaneous administration of glucose and of 10 to 12 units of insulin increased considerably the pyruvic acid content of the blood of three of the diabetic patients. The observations of the author thus corroborated those of the American investigators, i. e., that the pyruvic acid content of the blood in diabetic patients without ketosis undergoes the same variations as in normal persons. These observations lend support to the concept that in the absence of ketosis the glucose metabolism is normal in diabetic patients; the essential disturbance of the diabetic patient consists of the obstruction of the pathway of the glucose in entering the cell because of the total or relative insulin deficiency. The hyperglycemia thus is to be considered primarily as a defense process in which the liver plays the essential part; this process makes it possible to break through the cell barrier and finally to restore a relatively satisfactory balance. Determinations of the amount of pyruvic acid in the blood of diabetic patients with ketosis, acidosis, and coma revealed a normal pyruvic acid content if errors owing to the presence of acetoacetic acid were prevented by using a modified Friedemann-Haagen technique that makes it possible to eliminate the acetoacetic acid, leaving the alpha-keto acids unimpaired. Results showed that at the onset of diabetic coma and before the institution of treatment, the amount of pyruvic acid in the blood was about normal or somewhat lowered. It increased slightly after the administration of insulin and again became normal as soon as the patients recovered from coma.

Treatment of Diabetic Patients with Severe Acidosis.—Diabetic coma with severe acidosis occurring 28 times in 27 patients was treated with insulin. Of the 27 patients, 4 died but in only 2 of these was death attributable to ketosis, acidosis, and coma. The remaining 23 made a complete recovery. Of these 23, 6 were in a precomatose state with an alkali reserve between 20 and 30 volumes per cent, while 18 were unconscious with an alkali reserve below 20 volumes per cent. The insulin doses given to the patients varied from 80 to 680 units, except in one patient who had to be given more than 2,000 units. The average dose administered within the first 24 hours was 288 units. Treatment was begun with an intravenous injection of 30 to 40 units of insulin, an intramuscular injection of 40 to 60 units of insulin, and a subcutaneous injection of 60 to 100 units of protamine zinc insulin injection. The rationale of the combined use of ordinary insulin and of insulin with delayed but prolonged action was demonstrated by the satisfactory results obtained by the authors. Their results also demonstrated that the use of initial massive doses of insulin is not justified. This method involves some risks because it requires for the duration of the treatment the maintenance of a high concentration of glucose in the blood, thus exposing the patient to dehydration and to the loss of sodium that is needed for restoring the alkali reserve to normal. Artificial alkalization of the authors' patients by intravenous instillation of sodium bicarbonate seemed to be a valuable adjuvant to insulin. The usefulness of co-carboxylase as an adjuvant to insulin seems doubtful. It has been shown in the preceding paper that the increase in the pyruvic acid content of the blood in patients in diabetic coma was only apparent owing to the imperfect method used for its determination.

Ugeskrift for Laeger, Copenhagen

113:1537-1582 (Nov. 15) 1951

*Aureomycin and Chloramphenicol Treatment of Herpes Zoster. G. Schäffer and I. B. Svendsen.—p. 1537.

*Aureomycin Treatment of Recurrent Oral Aphthae. O. Gottlieb.—p. 1540.

*Terramycin Treatment of Otitis Media. J. C. Nielsen.—p. 1546.

Induced Abortion by Means of Partial Evacuation. P. Schou.—p. 1547.

Aureomycin and Chloramphenicol Treatment of Herpes Zoster.—In a given period Schäffer and Svendsen treated every other patient who had herpes zoster with aureomycin (500 mg. four times daily for four days) or chloramphenicol (from 2 to 4 gm. daily for from three to seven days). A total of 24 patients received antibiotic, and 22 control patients were given lactose

tablets. No difference was noticeable between the treated group and the control group with regard to the duration of the skin affection or neuralgias.

Aureomycin Treatment of Recurrent Oral Aphthae.—Gottlieb discusses rational treatment of oral aphthae on the assumption that they are due to activation of a latent virus infection. He reports 14 cases of long standing with free intervals of a month at the most, refractory to earlier treatment, in which aureomycin was given locally, mainly as a mouth wash. The result was good in 8 of the 11 cases of Mikulicz's solitary recurrent aphthae, and in Sutton's aphthae improvement occurred in two cases and one patient did not respond to the treatment. In two cases of multiple recurrent aphthae the treatment had no effect.

Terramycin Treatment of Otitis Media.—Terramycin treatment of 18 cases of acute otitis media and 2 of chronic otitis media gave good results. No complications followed, and side effects were seen in only five cases. Comparison with a corresponding series treated with penicillin showed terramycin to have the same effect as penicillin on pneumococcus otitis, not so good an effect as penicillin on otitis due to hemolytic streptococci, and better effect on otitis due to Pfeiffer bacilli. Since hemolytic streptococci and pneumococci are strongly sensitive to penicillin, Nielsen concludes that terramycin should be used against penicillin resistant bacteria of every kind, particularly gram negative rods. Examinations of resistance showed terramycin to be strongly or moderately active against all the bacteria found, both of primary and secondary etiologic significance, except *B. fluorescens* and *B. pyocyaneus*, which were weakly sensitive to terramycin, and *P. morganii*, which was resistant.

Wiener klinische Wochenschrift, Vienna

63:915-934 (Dec. 7) 1951. Partial Index

*Therapy in Rheumatic and Other Diseases of Joints with Implantations of Thyroid Tissue. F. Mandl and W. Gyri.—p. 916.

Five Years of Antibiotic Treatment in Accident Surgery. G. Salem.—p. 918.

Relationship Between Cervical Mucus and Sperma with Particular Consideration of Simm's-Hühner and Miller-Kurzrok Tests. G. Narik and A. Rockenschaub.—p. 922.

Thyroid Implantations in Diseases of Joints.—Various diseases of the joints in 50 patients, 29 with primary chronic polyarthritis, 1 with secondary chronic polyarthritis, 8 with arthritis deformans, 8 with spondylarthritis ankylopoietica of moderate degree, and 4 with spondylarthritis associated with sciatic pain, were treated by implantations in the abdominal wall of 5 gm. of thyroid tissue obtained from other patients during thyroidectomy. Complete recovery resulted immediately in 26 patients; definite improvement was obtained in 15 patients and slight improvement in 3; and in 6 patients the therapy failed. Of the 44 patients between the ages of 22 and 73 who had obtained satisfactory results and were followed for 12 to 22 months, 8 had recurrences. Of the remaining 36, 3 were free from complaints for 21 months, 1 for 20 months, 2 each for 19 and 17 months, 5 for 16 months, 9 each for 15 and 14 months, 3 for 13 months, and 2 for 12 months. Seven of the eight patients with spondylarthritis ankylopoietica and two of the four with spondylarthritis associated with sciatic pain obtained symptomatic relief. Four of five elderly former athletes with post-traumatic arthritis had good results. Compared with treatment with corticotropin (ACTH) and cortisone and treatment with corticotropin and vitamin C, this method has the following advantages: Improvement may be obtained with a single implantation of thyroid tissue for longer periods than with continued treatment by the other methods. Undesirable endocrine or allergic side-effects were not observed. The method is less expensive than the other methods and may be used in hospitalized as well as ambulatory patients. It is suggested that the effective thyroid implants neutralize the thyrotropic hormone of the pituitary and stimulate more profuse secretion of corticotropin. Changes in adrenal cortex function were demonstrated by the rapidly decreased number of eosinophils in the blood of the patients who obtained satisfactory results from the thyroid implantations.

BOOK REVIEWS

Cancer Cytology of the Uterus: Introducing a Concept of Cervical Cell Pathology. By J. Ernest Ayre, M.D., Director, Dade County Cancer Institute, Miami, Fla. Cloth. \$14.50. Pp. 407, with 362 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1951.

The objective of this book is to provide composite evidence of the character of cervical cancer, particularly in its early stages, by illustrating the clinical findings, the cytological manifestations, and the decisive histological studies in individual cases. The chapters concern the following subjects: development of concept, techniques in common use in gynecology, classification of normal cell types, inflammatory cell types, chronic cervicitis, early anaplastic cells, precancer cell complex, preinvasive carcinoma (carcinoma in situ), epidermoid carcinoma of the cervix, adenocarcinoma and other genital malignancies, and techniques for total biopsy (ring biopsy histological method).

The author maintains that a negative reaction from a surface cell biopsy, properly taken and interpreted, is the most accurate test available today to indicate the absence of cancer of the cervix. In one series of 155 patients with cervical cancer, reported from the Royal Victoria Hospital, the cell method missed 3 cases, whereas the tissue method (first biopsy) missed 15. Although a positive vaginal smear is highly reliable, a negative vaginal smear is not.

Ayre believes there are three predisposing factors in the pathogenesis of cancer of the cervix: persistent estrogenic tissue concentration, thiamine deficiency, and chronic infection. He says that, since chronic infection or inflammation in the cervix is so common and cervical cancer is so rare, there must be other etiological factors necessary to produce carcinoma. Yet serial, cytological, and behavior studies of cells and tissues known to have chronic inflammation lead to the belief that there is a sound etiological relationship between the two pathological states. There is strong disagreement with Ayre concerning persistent estrogenic tissue concentration and thiamine deficiency as possible causes of cervical cancer.

The author mentions Hellman's study of 290 pregnant women in whom routine punch biopsies of the cervix were performed. In six cases (2%), a diagnosis of intraepithelial carcinoma was made, and all of these cervixes were normal postpartum. Likewise, a follow-up examination of 6 to 18 months revealed normal biopsies. Discussing this study, Ayre confidently states, "Had biopsy been avoided and serial cell study by 'surface biopsy' substituted, conclusions could be more definite."

This book is far more an atlas than a textbook, because there is relatively little text material as compared with the space devoted to illustrations. There are 79 illustrations in color. All the illustrations are beautiful and clear. Acknowledgment for some of the illustrations is given to several pharmaceutical and other companies. At the end of the book is a useful section on definitions of common cytological terms and also a well-selected bibliography. The book has merit, and a large share of it is due to Papanicolaou, the founder of modern cytology.

Tonsil and Allied Problems. By Roy H. Parkinson, M.D., F.A.C.S., Chief of Eye, Ear, Nose and Throat Department, St. Joseph's Hospital, San Francisco, California. Cloth. \$12. Pp. 432, with 250 illustrations. The Macmillan Company, 60 Fifth Ave., New York 11, 1951.

This is the most extensive treatise that has been written on the tonsil and disease conditions in which tonsil infections may play a role. The book is well written and easy to read, and the illustrations are good. Most of what is said has been said before. The author utilizes 426 references.

The author errs in his reference to a quotation from another writer whom he credits with a statement to the effect that one-third of all operations performed on the urban population of this country since 1924 were for the removal of tonsils and

adenoids. That writer said that, in 1929, it had been reported that one-third of all the operations performed since 1924 were for tonsils and adenoids. (The incidence of tonsil and adenoid surgery is undoubtedly less than it was 25 years ago, and certainly less in proportion to other surgical procedures).

Approximately one-third of the treatise (146 pages) is devoted to the discussion of the structure, the embryology, and the gross and histological anatomy of the tonsils; five pages sum up what is known about tonsil physiology. The anatomic illustrations are excellent and are apparently original; some are in color. The next 172 pages are concerned with acute and chronic inflammatory diseases of the tonsil, tumors involving the tonsil and adenoid regions, and miscellaneous conditions that may involve the tonsils, such as hyperkeratosis, the relationship of certain branchial fistulas, the elongated styloid process, and glossopharyngeal neuralgia. Indications, technique, the care of the patient, and complications are discussed in the final 104 pages.

Some of the author's statements will be challenged, such as: "In cases of generalized and persistent bleeding x-ray treatment of the spleen will, in the large majority of cases, bring coagulability of the blood to normal," and "Recurrences are very common in children who have been operated very young." The author fails to differentiate between the ingrowth of lymphoid follicles into what was a previously clean fossa and a tonsil tag or remnant left at time of surgery.

This book serves a useful purpose by emphasizing the need for special skill in tonsil surgery, which is not a procedure to be taken lightly.

Proceedings of the Midcentury White House Conference on Children and Youth. Edward A. Richards, general editor. Report of conference sessions, Washington, D. C., December 3-7, 1950. Cloth. \$4. Pp. 363. Health Publications Institute, Inc., Raleigh, N. C., 1951.

This is the official report of the papers presented and the discussions reported at the fifth White House Conference on the problems of children. This conference brought together persons of many backgrounds and points of view to discuss "how we can develop in children the mental, emotional, and spiritual qualities essential to individual happiness and to responsible citizenship and what physical, economic, and social conditions are deemed necessary to this development." The material in this report includes selected addresses given before general sessions by outstanding speakers who discussed healthy personality development in children; selected technical papers dealing with certain critical aspects of personality development; and summaries of the 31 panels and the 35 work groups. The work groups were divided into five broad areas concerned with furthering healthy personality development in children and youth, furthering healthy personality development through social institutions, making more positive the influence of religious, social, and economic forces on personality development of children in special situations, and mobilizing citizens for the development of conditions affecting personality development.

Regardless of one's personal attitude toward the administration and the federal agencies responsible for this Mid-Century White House Conference, it must be recognized that basically it was in the tradition of the four previous conferences. The thinking of the 6,000 persons who attended the conference meetings and of the 100,000 persons who contributed to the conference in some way at the state and local levels was largely a sincere effort to improve the mental health of children. Any physician or, for that matter, any person concerned with other professional fields, who may have occasion to deal with children either individually or in groups, should be acquainted with what came from the Mid-Century White House Conference. Many state programs will be developing as a result of this conference. They will need the advice and counsel of the physicians in the communities of those states. To attempt this guidance without some knowledge of what has gone before will place physicians

at a disadvantage in dealing with other professional workers who are better informed.

The book is stimulating and interesting and contains a wealth of material. Though some persons may differ with the point of view expressed in certain portions of it, nevertheless, they are points of view that are current and that should be known, even though they might not be acceptable.

A Dictionary of Antibiotics. Compiled by Leonard Karel and Elizabeth Spencer Roach. Cloth. \$8.50. Pp. 373. Columbia University Press, 2960 Broadway, New York 27; Oxford University Press, Amen House, Warwick Sq., London, E.C.4, 1951.

The title of this book is most appropriate. Inasmuch as the term antibiotic is regarded by the authors as applicable to any substance derivable from living organisms and capable of adversely modifying the vital functions of specific microorganisms, information on a vast number of substances is provided in a necessarily brief, dictionary style.

The book is primarily designed to serve as a comprehensive and authoritative reference manual for investigators interested in the general field of fundamental antibiotic research; it serves a useful purpose as a valuable repository of obscure knowledge. The data are arranged alphabetically and consist of (1) a compilation of substances tested for antibiotic activity, (2) the available information on source, extraction, chemical and physical properties, spectrum in vitro and in vivo, toxicological, pharmacologic, and clinical and experimental results, and (3) an enumeration of organisms (designated as test organisms) against which substances have been tested for antibiotic activity. A comprehensive bibliography is appended.

The average physician will find this book of little practical value, inasmuch as the antibiotics that are available to him for clinical use receive far more detailed consideration and evaluation in other current publications.

Factors Regulating Blood Pressure: Transactions of the Fifth Conference, February 15 and 16, 1951, New York, New York. Edited by Benjamin W. Zweifach and Ephraim Shoor. Cloth. \$3.75. Pp. 238, with 49 illustrations. Josiah Macy, Jr., Foundation, 565 Park Ave., New York 21, 1951.

Eleven contributions by different authors make up this volume, each paper being accompanied by a report of the oral discussion that followed the reading of the paper. Most of the papers deal with biochemical and physiological research on the state of the blood and vessels in hypertension, arteriosclerosis, and atherosclerosis; much of the work concerns the possible role of cholesterol in these disorders. Much information is given, but frequently, it is of such a baffling and inconclusive nature that the reader wishes that the volume would close with a summary of some points on which agreement had been reached. A commendable feature is the cumulative index, which is indispensable in locating items discussed in this volume and the preceding four volumes. The book will be of value mainly to those engaged in clinical and laboratory research on the three disorders discussed.

Your Diabetes: A Complete Manual for Patients. By Herbert Pollack, M.D., Associate Physician for Metabolic Diseases, Mount Sinai Hospital, New York, and Marie V. Krause, M.S. Second edition. Cloth. \$3. Pp. 212. Paul B. Hoeber, Inc., (medical book department of Harper & Brothers), 49 E. 33d St., New York 16, 1951.

This is a manual designed to improve the diabetic patient's understanding of the nature and treatment of this disease. This book is written in a popular style; the chapters are short; the language is simple and direct; and the subject coverage is varied. Typical chapter titles are "What Insulin Does for You" and "You Can Live a Normal Life." The style is that of a physician giving instructions to an uninformed but intelligent diabetic patient. There are many manuals for diabetic persons. Each is written primarily for the patients in the author's practice and gains wider circulation according to its merit and need. Dr. Pollack's primer tells a story that has been told many times. Its usefulness, outside of his own practice, will be limited by the popularity of its competitors. The friendly manner and fresh approach of this book may justify its inclusion in the field. It is authoritative, interesting, and even dramatic in spots and, above all, new.

Any Questions? A Selection of Questions and Answers Published in the British Medical Journal. First Series. Cloth. 7s.6d. Pp. 240. British Medical Association, Tavistock Sq., London, W.C.1, 1951.

Eight years ago, the *British Medical Journal* began publishing a section in which answers were provided to questions submitted by medical practitioners. The questions were answered by specialists in the subjects concerned. The British editors have received many requests for a book containing these questions and answers, and this pocket size book contains the first selections made from this material. If it meets with approval, the editors plan to publish subsequent volumes each year. The first volume has the questions' and answers arranged alphabetically under general headings; for example, the questions on the first few pages pertain to the general subject of allergy, followed by questions on anesthesia and so on through the book, which ends with questions about sterilization, thermometers, and Turkish baths. There is a table of contents showing the pages on which the general subjects begin and an index, which makes detailed information readily available.

THE JOURNAL publishes a book of this nature under the title of "Questions and Answers"; the third volume was published in 1950.

Marriage, Morals and Medical Ethics. By Frederick L. Good, M.D., LL.D., and Reverend Otis F. Kelly, M.D. Cloth. \$3.50. Pp. 202. P. J. Kenedy & Sons, 12 Barclay St., New York 8, 1951.

The title fully covers the contents of this book. Written by two Roman Catholic physicians, one of whom is also a priest, and bearing the imprimatur of Archbishop Richard J. Cushing of Boston, it is a statement of the views of the Catholic church on matters in the medical realm that impinge on the doctrine held by the church. The subjects discussed include marriage, sex education, sex life of the person in and out of marriage, celibacy, interruptions of pregnancy for therapeutic reasons, surgery and therapeutics in pregnancy, with special reference to malignant growths involving the female generative organs, the "rhythm" theory as a contraceptive measure and as a way of life in marriage, and artificial insemination. The book is clearly and simply written and gives positive information as to the precise reasoning by which the church arrives at its position in these matters. It is written for physicians, clergy, lawyers, nurses, and social workers, generally, anyone who wants this information in authoritative form. Whatever the viewpoint of the reader, the book serves these stated purposes well.

Human Physiology. By Chandī Charan Chatterjee, B.Sc., M.D., Examiner in Physiology, M.B., B.S., University of Calcutta. Cloth. 45s; 22 rupees 8 annas. Pp. 813, with 141 illustrations. U. N. Dhur & Sons, Ltd., 15 Bankin Chatterjee St., Calcutta, 1951.

The author has made an effort to select, from the expanding universe of physiology, the things that a medical student needs to know most and can hope to assimilate. This book, therefore, contrasts most favorably with a number of other recent works that are written without regard for the pressure under which medical subjects are taught. This book is neither an exhaustive treatise nor a synopsis; it is a textbook, and many features, including the choice of type and arrangement of headings, are well calculated to aid the student. A considerable amount of histological and biochemical information that contributes to the clarity of the text is included.

This being a first edition, it is hoped that certain features may be improved in future printings. The dust cover and table of contents promise something on the increasingly important subject of biophysics, but the material on pages 56 to 59 is not at all representative of biophysics. This weakness is also exemplified in the unenlightening definition of a decibel (page 765) as one tenth of a bel and in the confusing and useless discussion of theories of color vision (page 763). Another point of contention relates to the terminology of neuroanatomy, namely, the continued use of phrases like "the tract of Goll" for the fasciculus gracilis. In the absence of a concerted effort by other teachers to eliminate these eponymic phrases, a courageous writer can do something by eliminating them from his own works. This book is recommended to all teachers and students of physiology.

Planned Parenthood: A Practical Guide to Birth-Control Methods. By Abraham Stone, M.D., and Norman E. Hines, Ph.D. Introduction by Robert L. Dickinson, M.D. Revised edition. Cloth. \$3.75. Pp. 221, with 26 illustrations. Viking Press, Inc., 18 E. 48th St., New York 17, 1951.

This volume is intended to be recommended to patients, by physicians, as a supplemental source of information on the problems of birth control, abortion, and sterility. Originally published in 1936 as "Practical Birth Control," it is now in its eleventh printing. The change in titles reflects a change in concept to emphasis on a suitably sized and spaced family rather than birth control procedures alone.

Regardless of one's feelings regarding the moral implications of birth control, one must recognize that a large portion of the laity practices child spacing. The public, therefore, requires information on control measures that will not damage future child bearing or the health of either marital partner. Most of the text is devoted to discussions of the social, legal, and medical aspects of birth control as well as the allied problems of abortion, sterilization, and infertility. The style is clear and objective but unimaginative, and the material included furnishes the requisite information.

The objectivity of the text is, to a certain extent, lost in the last chapter on the planned parenthood center. The authors, as prominent members of the movement, naturally seek to foster and defend its program. In their zeal, they make scant reference to the role of the family physician as the most frequently consulted advisor on child spacing and infertility problems. Indeed, the task of the physician is surrounded with an unrealistic aura of specialization that is not warranted by the relatively simple procedures involved. Finally, acceptance of patients from the upper income brackets on the flimsy excuse that they are unable to find a private physician properly qualified seems indefensible and a violation of usual free clinic practice.

Cerebral Mechanisms in Behavior: The Hixon Symposium. Edited by Lloyd A. Jeffress, Professor of Psychology, University of Texas, Austin. Cloth. \$6.50. Pp. 311, with illustrations. John Wiley & Sons, Inc., 440 Fourth Ave., New York 16; Chapman & Hall, Ltd., 37-39 Essex St., Strand, London, W.C.2, 1951.

In September, 1948, a group of scientists met at the California Institute of Technology to discuss "Cerebral Mechanisms in Behavior." The report of the five day conference, edited by the professor of psychology at the University of Texas, is now issued. The principal speakers were John von Neumann, Warren S. McCulloch, K. S. Lashley, Heinrich Klüver, Wolfgang Köhler, and Ward C. Halstead. In addition, there was a discussion panel of well-known physiologists and neurologists. The stenographic report, including the discussion, was submitted to each speaker for revision before the final editing. The topics considered, brain and intelligence, relational determination in perception, the problem of serial order in behavior, and why the mind is in the head, were of general interest. This symposium, financed by the Xon Fund, is valuable as a record of the considered opinions of leading authorities. The editor, in compiling the report, has removed irrelevant material and particularly repetitions, has presented a readable text. This has taken some time, but the importance of the subjects discussed as well as the useful illustrations and ample references justify publication, in 1951, of a conference that took place in 1948. The book will be of value to psychologists, psychiatrists, and all clinicians who have a particular interest in the field of neurology and psychiatry. A photograph of the participants is used as a frontispiece. There are adequate name and subject indexes.

Pathology of the Eye: A Practical Treatise of Histopathology. By J. B. Fuchs, M.D., Consulting Ophthalmologist, New York Hospital, and Adalbert Fuchs, M.D., Consulting Ophthalmologist, New York Eye and Ear Infirmary. Cloth. \$20. Pp. 420, with 1140 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33d St., New York 16, 1952.

Two eminent eye pathologists, one with an American and the other with a European background, but both students of the late Ernst Fuchs, have united their talents to produce an authoritative textbook on ocular pathology. Profusely illustrated with beautiful drawings (including nearly 200 in full color) and well printed on a good grade of paper, this volume is an outstanding example of the bookmakers' art. The text is adequate, lucid, and practical, without being verbose. It is much more than an exposition of pure basic ophthalmic pathology, since there is emphasis on the practical clinical applications and implications of the histopathological changes described and illustrated. It is of value, therefore, to the practicing ophthalmologist, whose primary interest is clinical, but who realizes that his understanding of ocular disease is accentuated by an appreciation of the correlation between the gross clinical picture and the microscopic histopathological findings. To the general pathologist, whose knowledge of ocular pathology is often too meager, this work will prove to be of inestimable value.

In addition to separate chapters on general pathology, the cornea, uvea, sclera, lens, retina, optic nerve, and vitreous, special sections are devoted to myopia, tuberculosis, syphilis, postoperative complications, injuries, and tumors. The ophthalmic surgeon will find the chapter on postoperative pathological findings and their complications particularly illuminating and practical.

There has long been a need for a modern, adequate, and accurate textbook in English dealing with pathology of the eye. By not only presenting such an atlas but in addition bringing the clinic and the laboratory together, a real service has been rendered to ophthalmology. It is likely that this book will remain the standard authority in the field for a long time.

Dible and Davie's Pathology: An Introduction to Medicine and Surgery. By J. Henry Dible, M.B., F.R.C.P., Professor of Pathology in University of London, London. Third edition. Cloth. \$13. Pp. 963, with 417 illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; J. & A. Churchill, Ltd., 104 Gloucester Pl., Portman Sq., London, W.1, 1950.

This textbook was written to assist medical students who are studying human pathology for the first time. The style, scope, and content of the book indicate that the authors have had considerable experience in teaching elementary pathology. Photographs and drawings are good and well chosen. The important aspects of the subject are clearly and concisely discussed, and detailed analysis of controversial points is omitted. Care is taken in the definition of terms, although some terminology, especially that concerned with the classification of tumors, is misleading and not generally accepted. A creditable attempt has been made to create a better understanding of the relationship between the structural changes in disease and other pertinent scientific facts. As is usual in elementary textbooks, this attempt falls far short of its objective. There is too much to be presented and too little space to present it in. The lack of a bibliography detracts from the usefulness of the book. A good bibliography is needed by the exceptional student in the beginning and by all students who wish to comprehend the more intricate aspects of pathology as they gain clinical training and experience. Briefly, this textbook is as good as many others written for a similar purpose. Criticisms are levelled at the lack of a broader purpose, namely, the support of a continuing interest in pathology as the most objective point of departure for an understanding of the disturbances caused by many human diseases.

Principles and Practice of Obstetrics. Originally by Joseph B. DeLee, M.D. By J. P. Greenhill, M.D., Attending Obstetrician and Gynecologist, Michael Reese Hospital, Chicago. Tenth edition. Cloth. \$12. Pp. 1020, with 1140 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1951.

This completely rewritten and revised edition continues on the high plane of its predecessors. This volume, divided into two major parts, is excellently and copiously illustrated with diagrammatic, histological, and pathological plates in black and white and color. The first half of the book is concerned with the physiology of reproduction, pregnancy, labor, and the puerperium; the second half discusses the pathology of pregnancy, labor, and the puerperium. The style is clear, lucid, and interesting. The terms employed are those agreed on by the authors of the principal obstetric texts. The treatment recommended is conservative and logical and reflects the methods of the senior author. The new edition, in toto, is a worth-while addition to any library and is an excellent textbook for the student and practitioner.

The Clinical Method in Psychology. By Robert I. Watson. Washington University School of Medicine, St. Louis. Under editorship of Gardner Murphy. Cloth. \$5. Pp. 779. Harper & Brothers, 49 E. 33rd St., New York 16, 1951.

This book is designed primarily as a graduate text in clinical psychology. The author emphasizes that clinical methods in psychology, as conceived today, consists of applications of psychiatric principles and therapy that have been drawn from an overall body of literature that stems from dynamic findings in the fields of psychology, personality studies, psychotherapy, psychoanalysis, and anthropology. The recent trend toward a dynamic approach to psychology is considered mainly the result of Freud's influence.

The author describes clinical methods in child guidance, student guidance, personal guidance, and personnel guidance in industry. A large section of the book is devoted to diagnosis; several projective methods, including the Wechsler-Bellevue Intelligence Scale, the revised Stanford-Binet test, and the Vineland Maturity Scale are described. The author has specifically omitted the Rorschach and many other projective diagnostic tests because they are sufficiently covered in other textbooks. About one-third of the book is devoted to the discussion and demonstration of the variability in psychotherapeutic method. Chapters on child psychotherapy and group psychotherapy are of considerable practical value.

The Study of Instinct. By N. Tinbergen. Cloth. \$7. Pp. 228, with 130 illustrations. Oxford University Press, 114 Fifth Ave., New York 11; Amen House, Warwick Sq., London, E.C.4, 1951.

This extraordinary book assembles a multitude of facts regarding the objective behavior of animals, especially in regard to untaught, innate, or instinctive activity. The subject matter has great intrinsic interest, but it acquires added importance from the applications to human behavior sketched by the author in the concluding pages (page 205 ff.). The occurrence of certain errors is a conspicuous and almost inevitable characteristic of instinctive behavior; this is illustrated by a beetle caught in a physiological trap (page 26). In the realm of the reproductive functions, in particular, results of great significance have been obtained; an example is the extent to which substitutes for the normal stimulus will release a given pattern of response (page 115). The course of recent history clearly shows that survival of the human race depends on our ability to understand human behavior, to tolerate deviations, and to guide each other into constructive channels. This book is a substantial contribution to such understanding; it is earnestly recommended to criminologists, psychiatrists, and psychologists as well as to health educators, counsellors, and others who undertake to influence the behavior of their fellow men.

The World's Best Doctor Stories. Edited by Noah D. Fabricant, M.D., and Heinz Werner. Cloth. \$2.50. Pp. 276. Garden City Books, Garden City, New York, 1951.

Probably no two persons agree on what stories should be included in a book of this type; for this reason, it is permissible to state that there are some good, some fair, and some indifferent examples to be found. Some stories, such as Poe's "horror" on mesmerism, are considerably less shocking to an adult than to a young, wide-eyed reader, as is Balzac's tale of the atheist surgeon who unaccountably founded a special mass. Perhaps the most interesting feature of the book is the opportunity it affords one to muse on the public's attitude toward physicians. Most of the contributions show a friendly attitude; a few, however, do not. The 24 selections run the gamut from tragedy, pathos, and stark realism to humor, gaiety, and the mystic. With such variety, every reader is certain to find enough to please him.

Renal Function: Transactions of the Second Conference, October 19-20, 1950, New York, N. Y. Edited by Stanley E. Bradley. Cloth. \$3. Pp. 178, with 31 illustrations. Josiah Macy, Jr., Foundation, 565 Park Ave., New York 21, 1951.

This small volume is a verbatim account of the Second Conference on Renal Function, sponsored by the Josiah Macy, Jr., Foundation. It consists of a series of seven reports by research workers in the field of kidney function. Each report is followed by a discussion and an exhaustive list of references. The discus-

sion of each report is informal and conversational and is often longer than the report itself. This style makes reading difficult, for the conversation often jumps abruptly from one phase of work to another. Most of the reports are concerned with the effects of various hormones on renal function, and one report deals entirely with corticotropin (ACTH) and cortisone. The book will be of value only to those who are engaged in research on kidney function. Most of the work described is still in the experimental stage and would not have practical value in the ordinary clinical or hospital laboratory.

Prescription Writing and Medical Jurisprudence. By Harold N. Wright, Professor of Pharmacology, University of Minnesota, Minneapolis. Fourth edition. Paper, loose-leaf. \$2.25. Pp. 114, with illustrations. Burgess Publishing Company, 426-428 S. Sixth St., Minneapolis 15, 1951.

In most instances in the relationship between the physician and the patient, the prescription is the contact point for therapy. It is the purpose of this well-organized manual to help instruct medical students in the fundamentals of this important facet of medical practice. In this edition the contents have been revised to accord with the titles and formulas of the current revisions of the official compendiums. In spite of the strong current trend toward the use of valuable new drug specialties, the emphasis in this manual remains on official drugs. For the purpose of teaching prescription writing, this is good, since controversy as to the merit of new drugs is avoided, and yet the manual affords opportunity for practice in writing suitable prescriptions for different forms of drugs. In view of the rapid decline in the use of Latin in prescription writing, the amount of space devoted to this subject seems excessive. The section on medical jurisprudence concerns mainly legislation governing the prescription of narcotic, hypnotic, and other dangerous drugs and with the medicolegal aspects of drug prescription.

Die Trübungsformen der menschlichen Linse. Von Dr. Hans Sautter, apl. Professor und Oberarzt an der Universitäts-Augenklinik Tübingen. Cloth. 49.80 marks. Pp. 139, with 191 illustrations. Georg Thieme, Diemshaldenstrasse 47, (14a) Stuttgart O; agents for U. S. A., Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1951.

This is essentially a small atlas depicting the commoner diseases of the human crystalline lens as seen and studied with the biomicroscope. Most of the illustrations are good reproductions of remarkably clear, accurate, and instructive drawings. The accompanying text is lucid and concise, stressing the morphological characteristics and the differential diagnosis of the various types of cataracts. The book is intended for and will be useful to graduate students and practitioners of ophthalmology to whom the larger atlases are not readily available.

Medizinische Terminologie: Ableitung und Erklärung der gebräuchlichen Fachausdrücke aller Zweige der Medizin und ihrer Hilfswissenschaften. Herausgegeben von Dr. med. Herbert Volkmann. Thirty-fifth edition, edited by Dr. med. Kurt Hoffmann. Cloth. 28 marks. 1130 columns. Urban & Schwarzenberg, Thierschstrasse 77, München 22; Meinekestr. 13, Berlin W. 15, 1951.

This edition has been thoroughly revised and brought up-to-date since the publication of the previous edition, eight years ago. It lists all important words, phrases, and names in current usage in medicine and the allied sciences, with their etymology, definitions, dates, and explanations. The main drawback is that the explanations are in German, and it requires more than a superficial knowledge of this language to make efficient use of this volume.

Parasitic Animals. By Geoffrey Lapage, M.D., M.Sc., M.A. Cloth. \$4. Pp. 351, with 113 illustrations. Cambridge University Press, Bentley House, 200 Euston Rd., London, N.W.1; American branch, 51 Madison Ave., New York 10, 1951.

The author discusses the different parasites, not as entities, but according to their modes of life, the way they develop, their entrance into the host, the effect of the parasite on the host, and the effect of the host on the parasite. The chapter on "Avoidance of the Parasitic Animal by the Host" is interesting, since it considers factors other than those usually included in prevention. The book is intended for general reading on the subject; it is readable and accurate and is recommended to persons who have a general interest in

tive, but, of six such cases successfully treated with streptomycin on the first, second, and third days of the disease, serum agglutinins appeared in all patients, and rose from 1:320 to 1:2,560 within two to three weeks after the onset. In treating tularemia, aureomycin hydrochloride, chloramphenicol, and terramycin hydrochloride, although clinically highly effective, are bacteriostatic, not bactericidal like streptomycin, and it is unlikely that any of these agents is more effective than streptomycin for antibody inhibition.

Difficulties are likely to occur in unproved cases. There was an odd, and apparently unique, appearance and disappearance of serum agglutinins in Pulaski and Amspacher's case 4 (*Am. J. M. Sc.* 214:144 [Aug.] 1947) after streptomycin therapy was given for an ocular infection that may have been tularemia. This may be true of your patient; however, there is no conclusive evidence in either instance. In the above discussion, it is assumed that the utmost confidence can be placed in serum agglutination test techniques and interpretations. With repeated testing, as described above, any titer, even one as low as 1:20 or 1:40, has significance, if it represents genuine agglutination.

TESTS FOR SYPHILIS

TO THE EDITOR:—1. Have any serologic tests for syphilis been developed that are more accurate than the Kahn test? 2. Are there any tests that are more apt to give a false positive result? 3. At what titer does a Kahn test assume significance?
John P. Gifford, M.D., Vero Beach, Fla.

ANSWER.—None of the three questions raised can be answered without qualification. 1. The accuracy of a test for syphilis has two aspects, sensitivity and specificity. A test having high sensitivity in the detection of syphilis is likely to have low specificity and to give a considerable number of false positive reactions. A test low in sensitivity is likely to be high in specificity. If only the question of the specificity of the Kahn test is considered, the answer might be found in the serologic results of the annual official evaluation surveys of tests for syphilis. These are carried out under the auspices of the National Advisory Serologic Council, U. S. Public Health Service. According to reports of this council, the Kahn test has given no false positive reactions in 15 such surveys conducted since 1937 (Kahn, R. L.: Serology with Lipid Antigen with Special Reference to Kahn and Universal Reactions, Baltimore, Williams & Wilkins Company, 1950, p. 119). No other tests, including those employing a cardiolipin antigen, showed as high a record of specificity in these surveys. The spirochetal immobilization test of Nelson and Mayer (Immobilization of Treponema Pallidum in Vitro by Antibody Produced in Syphilitic Infection, *J. Exper. Med.* 89:369, 1949) is probably more specific than any of the serologic tests involving lipid antigen, including the Kahn test. However, this test is relatively low in sensitivity in early syphilis (Nelson, H. J., and Thompson, F. A. Jr.: Treponemal Im-tion Test of Normal and Syphilitic Serums, *J. Ven. Dis.* 30:309, 1949) and is, as yet, extremely difficult to perform. It should not be assumed from the high specificity record of the Kahn test in official evaluation studies that the test is free from false positive reactions. There is no test for syphilis carried out with lipid antigen that does not in certain instances give such reactions. Therefore, positive serologic reactions in the absence of clinical and epidemiological evidence of syphilis should always be interpreted with caution. Regarding sensitivity, the annual surveys have reported that other serodiagnostic tests at times have higher sensitivity than the Kahn test, especially in treated cases of syphilis.

2. It is difficult to say which tests are more apt to give false positive results. According to the reports of the above-mentioned surveys, a test that gives false positive reactions in a given survey may give none in several other surveys and then give several in a subsequent survey.

3. In a person with a lesion suggestive of early primary syphilis, even a doubtful serologic reaction may be highly significant, because, in a matter of days, this borderline reaction may prove to be the forerunner of a strong reaction of high titer associated with syphilis. On the other hand, in a person in whom clinical and epidemiological studies indicate absence of syphilis, a relatively high titer, such as positivity in 1:8 or 1:16, is

dilutions, may not prove significant, especially when the titer gradually drops to negativity spontaneously, suggesting a false positive reaction. It is safe to interpret positive reactions given by serologic tests for syphilis only in relation to clinical and epidemiological observations.

SURANYI'S CANCER TEST

TO THE EDITOR:—Please tell me the technique for performing Suranyi's test for the albumin reaction for the diagnosis of carcinoma.
Philip Norman, M.D., New York, N. Y.

ANSWER.—The Suranyi test is based on the idea that certain acids enable iodine in potassium iodide to precipitate the proteins more readily in the serum of cancer patients than in that of normal subjects. Suranyi used hydrochloric acid, acetic acid, or sulfosalicylic acid. According to Homburger's review (Evaluation of Diagnostic Tests for Cancer: Methodology of Evaluation and Review of Suggested Diagnostic Procedures, *Cancer* 3:143 [Jan.] 1950) there is no particular merit to this test. Its original description may be traced back through the references given by Homburger.

LOW SALT DIET AND HYPERTENSION

TO THE EDITOR:—I have been on a low salt diet because of hypertensive heart disease. Nonprotein nitrogen is normal, and there is no decompensation. It has occasionally been my custom to take "Sal Hepatica" and, oftener, a glass or two of "Saratoga Geyser" water, containing sodium chloride and sodium bicarbonate among other ingredients. Could either of these products prove harmful under such circumstances?
Reginald Van Woert, M.D., Rabena, N. Y.

ANSWER.—The salt content of the diet need not be so strictly controlled in the treatment of congestive heart failure, but, if the intent is to reduce blood pressure and so spare the heart, restriction of salt must be severe. The use of saline cathartics or mineral waters would thus defeat the latter aim and probably jeopardize the former. It is certainly better to err on the side of too little salt than take chances with too much.

ALLERGY

TO THE EDITOR:—I believe that most of the colds referred to in the answer to the question on allergy in THE JOURNAL (147:1399 [Dec. 1] 1951) are caused by food allergy rather than by infection. The initiation of the allergy in the nose results in symptoms suggesting a head cold, which are associated or followed in a few hours or a day by allergic bronchitis or asthma. The fever, often present for one or two days, may also be caused by food allergy. When fever and bronchial symptoms continue for four or more days, a secondary infection may have developed. When food allergy is controlled, infectious colds usually occur without asthma, thus disproving the idea of infectious asthma. Inhalant allergy, at times associated with food allergy, must be properly treated. It, however, rarely causes cyclic attacks of asthma initiated by colds.

I have, for many years, reported on the frequent decrease of nasal and bronchial allergy caused by foods, during the summer. Its reactivation between late August and December reestablishes the recurrent colds with allergic bronchitis or asthma. If the food allergy is not recognized, infection is usually assumed responsible and the condition incorrectly diagnosed as infective asthma. The study of food allergy by use of my cereal-free elimination diet, modified according to published directions, has confirmed the above conclusion. To establish this theory, it was usually necessary to use this diet, which excludes all cereals as well as milk, eggs, chocolate, fish, and other less allergenic foods, rather than a simple wheat, milk, and egg-free diet. Failure to use this diet accurately, to insist on strict exclusion of traces of excluded foods, and to continue the diet for adequate periods, while possible food allergy was studied, accounts for the failure to recognize the role of food allergy, which is equally important, in my experience, to inhalant allergy and infective asthma.

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